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Table of Contents.

PINK DISEASE: AN INVESTIGATION OF ITS CAUSE AND TREATMENT. (PRELIMINARY REPORT.)

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THIRTY-FIVE YEARS have passed since the attention of the medical world was first drawn by Dr. H. Swift, of Adelaide, to pink disease—an obscure, exasperating, yet fascinating disease. He first recognized the disease when he was a house physician at Great Ormond Street Children's Hospital, London in the year 1885. In the years from 1912 to 1914 he collected and studied 14 cases, the symptoms and signs of which he described at the Australasian Medical Congress, Auckland, New Zealand (1914). He called the disease "erythrœdema". Although he greatly aroused the interest of his audience, unfortunately his paper was not widely distributed throughout the world. He defined the disease as "one characterized by swollen, bluish red hands and feet, disordered digestion, followed by considerable muscular paresis, occurring in children between the ages of six and sixteen months". (It was found later that the age grouping extended beyond these limits.)

Swift realized that some of these infants were bottle-fed, others breast-fed; he noted that there was a derangement of the alimentary tract with anorexia, that the hands and feet were swollen, red, cold and clammy, that itching was often severe, and that the child might tear at itself. He also noted the fact that the redness did not extend beyond the wrists or ankles. The miliarial rash, the flaccidity of the muscles, the profuse sweating, the insomnia, the restlessness and the irritability were all familiar to him. He pointed out that recovery was slow, but that if it took place it was complete; also that feeding these children was of great importance.

To Dr. Swift should go the credit of first giving an adequate picture of this disease and of arousing the interest of the Australian medical world, although he was not the first man to describe it. Selter of Germany (1903), at a congress in Cassel in 1903, made reference to eight cases of a disease he termed "trophodermatoneurosis". He was at a loss to find any description in the literature comparable to it. His accurate paper aroused little interest and was not brought to the light of day until Rocaz of Bordeaux (1933) drew attention to it.

This disease had not entirely escaped notice prior to Swift's paper. As Wood and Wood point out (1935), in 1883 William Snowball of Melbourne talked of "raw beef hands and feet", while Charles Clubbe of Sydney, at about the same time, coined the name "pink disease" for this condition. A. J. Wood brought forward the case histories of three children between 1898 and 1901 after searching back through his case records. Littlejohn (1923) also had been aware of the condition.

This disease was also independently described by Bilderback of America in 1920, and for the second time in Germany in 1922 by Feer. Both were unaware of Swift's publication. Bilderback had collected ten cases over the previous six years, and he presented a paper before the North Pacific Pediatric Society, Seattle, Washington. He pointed out the afebrile nature of the disease, and the fact that these children, if of a walking age, immediately stopped walking, that their muscles were weak and that the children were exhausted, wanting only to lie in bed. He pointed out also, that a psychological change often occurred—that these children might cry with rage at the sight of their closest relative. He noted that most came from good homes with apparently good food. He con-

cluded that "in the absence of temperature I could hardly consider an infection, but did consider a low-grade toxæmia or a deficiency disease".

Feer (1923) laid great stress on a dysfunction of the vegetative nervous system. He presented his paper before the Swiss Society of Pædiatrics in 1922, and in 1923 he made a further report in the *Annales de médecine interne et de pédiatrie.*

In England, Parkes Weber described the disease in 1921, and in France, Comby in 1922. In America other observers soon made further reports. Weston of Columbia (1920), giving the disease the name "acrodynia" (which it still bears in the United States), made a report. Byfield of Java City presented 17 cases (1920), and soon many reports by numerous men began to appear in the literature, some of the most important being by Brown, Courtney and MacLaughlin in 1921, by Vipond (1922), by Field (1922), by Zahorsky (1922) and by Paterson and Greenfield (1923-1924).

In Australia progress was being made, and at the first session after the 1914-1918 war of the Australasian Medical Congress, held in 1920 at Brisbane, A. J. Wood of Melbourne presented a report based on the study of 91 cases in conjunction with Hobill Cole. This report firmly established the symptomatology of the disease. Thus it can be seen that by the early 1920's this disease was rapidly becoming known and recognized throughout the world.

ÆTIOLOGY AND THEORIES OF CAUSATION.

Although the eight cases presented by Selter in 1903 were all among female children, it has since been shown that the sexes are affected equally.

The interesting point which grasps the attention is the age distribution of this disease—it is so sharply demarcated. Wood and Wood (1935) found that in their series of 116 cases, the majority, about 65%, were among children aged between nine and eighteen months, and although these workers had seen over 200 patients in Australia, they had all been aged under four years. I obtained similar results on looking into the age groups of 136 patients admitted over the last ten years to the Adelaide Children's Hospital (Cheek, 1949). Here 90% of the cases occurred in children aged between six months and two years, and 60% in children aged between ten months and eighteen months. Gareau (1946) in Canada, in his series of 75 cases, found the average age to be eleven months, the lowest five months and the highest three and a half years. In 65 cases presented by Fisher (1947) in England, 78% lay between six months and eighteen months. These results, however, do not agree with those quoted from France by Rocaz (1933) from his own series of 39 cases, or with those of Cosmi, who had 165 cases. In Rocaz's own series 71% occurred after the age of two years, and in that of Cosmi 51% occurred between the ages of two and eight years. It would seem from these figures that the majority of cases occur before the age of two years, but that in France the disease is manifested commonly in older children. Patients aged six weeks and fourteen years are on record (Rocaz, 1933). White (1926) reported two cases in adults.

The question of seasonal incidence has been raised and discussed. Woringer stated that pink disease was a disease of winter and spring (1926), and Braithwaite (1933, 1936) stated that in England there was a pronounced seasonal incidence in the spring and summer and that the disease tended to be more common in sunny countries. He stated that of 49 patients, only eight were admitted to hospital in the winter months. In direct contrast to this was the series of 89 cases of Cosmi in France (1930). His cases tended to be more numerous during the winter months. Wycoff denied that the seasons played any part (1929). This is the general opinion, and has been shown in Australia and England (Wood and Wood, 1935; Fisher, 1947).

Though the seasons play no part, geography apparently does. Australia, America, Canada, England, Central Europe and New Zealand seem to talk of and present more cases than the other countries of the world. One never seems to hear of cases coming from the Scandinavian countries. More interesting still is the regional distribution of this disease within countries themselves, as pointed out by Zechlin (1929), Rocaz (1933), Zahorsky (1922), Péhu and Boucomont (1936) and Nesbit (1932), and recently in England by Logan (1949).

Zechlin pointed to the south-west of Germany. Rocaz spoke of epidemic outbreaks which occurred in a group and seemed to bear a relation to the water courses in French territory. Zahorsky noticed the southern part of St. Louis. Nesbit drew attention to the increased incidence in the north of the United States and Canada. Logan, by a detailed study of the mortality rates in England from 1923 to 1947, showed that for the years 1940 to 1946 certain areas of England had a regional increase of incidence.

Although some may be sceptical, recurrences of this disease do take place.

There is the case of Dr. F. L. Wall in this city of Adelaide, of a child, Christine F., who in February, 1942, at the age of thirteen months, was admitted to Wade House, Royal Alexandra Hospital for Children, Sydney, suffering from pink disease. She had photophobia, anorexia, insomnia, redness of the hands and feet, ulceration of the gums, profuse sweating and loss of weight. She had a rash over her body, and although she had been walking at the early age of eleven months, she immediately ceased to do this and became listless and irritable. The mother, who is a trained nurse, first thought, as often happens, that the child was teething, and teething powders were administered. She was given "Vibex" injections and the condition persisted for six months. When the child was aged four years and ten months, the mother noticed her to be listless—"she just wanted to sit all day". She became "difficult and naughty" and on one occasion attacked her grandmother with a stick. She refused to eat and started grinding her teeth, and her hair went straight and started falling out. She began to sweat a lot, especially at night, and a slight rash developed. The child complained of pains in the legs and back, and her hands became red, and she frequently exclaimed that they were itchy and that she had "prickles" on her hands. She wanted to put her hands in water all the time. Again ulceration of the mouth developed and the muscles became weak. A psychological change became apparent by the fact that she used to upset her mother a great deal by saying "I hate you". She had the typical "mousy" odour. The condition again took six months to clear up.

Péhu of France (1941) found 25 cases of recurrences in the literature and reported two more. Zahorsky (1943) reported the case of a child, aged fifteen months, who had the disease with the complete picture, which lasted for twelve months; again at the age of five years the child contracted the disease, which lasted for six months. In the second attack she again developed the complete picture, even to the looseness of the teeth, and she also manifested, interestingly enough, *petit mal* attacks and a convulsive seizure. This is not found very often, but it is quite conceivable on theoretical grounds, as I should like to point out later.

Identical twins may also contract the disease at the same time.

Theories of Causation.

Many different theories have been put forward to explain this disease. The ones holding most sway are (i) mercurial poisoning, (ii) infection, (iii) vitamin deficiency and (iv) dysfunction of the vegetative nervous system.

Mercurial Poisoning.

Warkany and Hubbard (1948) have shown an increased amount of mercury in the urine of 18 children out of 20 suffering from pink disease; of a control group, 80% passed no mercury in their urine. These writers suggested that these children have an individual susceptibility to mercury, and that since arsenical poisoning could produce a picture somewhat resembling acrodynia, the disease probably had more than one cause. Fanconi and Botszteju (1948) concluded that "mercury is probably the most common cause of Feer's Disease in children constitutionally prone to it", and Bivings and Lewis (1948) and Elmore (1948) claim good results from treatment with BAL.

However, one must realize that most mothers on observing the first signs of this disease immediately conclude that the irritability is due to teething trouble, so teething powders containing calomel are promptly administered. These children, for this reason, nearly always receive teething powders and consequently pass mercury in their urine. One would expect to find more mercury in the urine of these children than in the urine of others.

Infection.

Byfield (1920) postulated that a virus was the cause. He thought that the influenzal virus might manifest itself in children in this way. Vipond (1922) reported the cure of two patients by a vaccine obtained from aspiration of enlarged glands. Rodda (1925), after a review of 17 cases, thought that the ætiology was associated with a chronic upper respiratory tract infection and focal infection. He said he had never seen the condition in a child whose tonsils and adenoids had been removed, and reported speedy recovery in all cases after this treatment. Many feel that a respiratory infection is important in the ætiology. That a virus infection is responsible is perhaps the most strongly held view. Rocaz (1933) concluded his book as follows: "After reviewing all the available evidence I consider the facts are extremely suggestive that pink disease is an inflammation of the nervous system and bears an intimate relationship to epidemic encephalitis." Littlejohn (1923) states that the condition is due to an infection of the nervous system involving in particular the vasomotor centres in the medulla and spinal cord. Case histories suggesting transmission of an infective agent are sometimes to be found. However, there are some important facts against an infective origin.

The patient is usually afebrile or only a low-grade pyrexia is present. No positive evidence has come from a study of blood cultures (Penfold, Butler and Wood, 1932). The sharply defined age grouping of this disease would seem to dispute infection. No definite change is found in the cerebro-spinal fluid as one might expect from a virus invading the central nervous system. Burnet of Melbourne (Wood, 1936) has tried every known method of culture for viruses without success; and above all, as pointed out by Gareau (1942), "in the hundreds of cases reported no mention is made of any sequelæ such as one would expect to find from organic disease in the central nervous system".

Vitamin Deficiency.

The realization has grown over the years that none of the known vitamins exert any specific effect on the course of this disease. Weston (1920) was the first to suspect one of the food elements. Some think the disease is the result of a quantitative rather than a qualitative deficiency of vitamins (McClendon, 1929, 1931), or that the factor is closely related to yeast or viosterol. Vitamin *B* complex, nicotinic acid and pyridoxin have all been tried. This disease occurs in breast-fed as well as in bottle-fed babies, and some of these children come from the best of homes with good food. Also the disease does not seem to occur in China or India where the standard of living is low and where the known deficiency diseases are more common.

Dysfunction of the Vegetative Nervous System.

The theory of vegetative nervous system dysfunction also has a large following, and was first initiated by Feer (1923), who thought it a functional disturbance. He considered that a vasomotor upset with severe sweating, coldness of the extremities, tachycardia, hypertension and dermatographia all evidenced this. Hutchinson (1932), Eley (1934), Cobb (1933), and Blackfan and McKhann (1943) have all pointed to the sympathetic nervous system. Others postulate an encephalic lesion localized in the mesencephalon and diencephalon.

Other Theories.

A reference to arsenical poisoning has already been made, but the age incidence is against this.

Braithwaite (1933, 1936) concluded that this disease was due to an increased sensitivity to sunlight following respiratory infection.

Mayerhofer (1938) put forward the idea that the disease might be due to spores of a cereal smut, which contaminated bread. This question was gone into in Australia by Clements (1940), and he showed the claim to be invalid.

PATHOLOGY.

In relation to the skin, hyperkeratosis and hyperplasia of the epidermis with atrophy of the subcutaneous adipose tissue, pigmentation of the rete, and hypertrophy of the sweat glands, were noted by Holt, Emmett and Howland (1936).

The pathology in respect to the nervous system is in a somewhat confusing state. In short, changes in almost all parts of the central nervous system have on occasions been described. Demyelination of the peripheral nerves, degeneration of the nerve cells in the brain and spinal cord and gross changes in the sympathetic chain have all been mentioned. Different pathological reports point to different regions of the nervous system.

Wyllie and Stern (1931) concluded their study of seven cases with the note that "in all cases the clinical symptoms were much in excess of the pathological findings". Further, some authorities (Mitchel Nelson, 1945) deny any significant changes in the nervous system. Also Warthin (1926) found meningeal irritation and œdema, but no change in the peripheral nervous tissue. Wolf, Paterson and Davison (1934) have cleared the picture somewhat by showing that the changes described could be produced by starvation alone.

I have been unable to find any significant changes in the cord and peripheral nervous tissue of a child who was in a good nutritional state and who died from circulatory collapse.

SYMPTOMS AND SIGNS.

There are severe and mild forms of this disease. The severe cases are obvious at a glance. The mild ones, unless observed carefully, are often missed, particularly if the redness of the hands and feet does not occur or is late in presenting. Abortive forms also occur. The onset of the disease is insidious. Often there is a history of some preceding infection with elevation of the temperature, and the mother, noticing the baby to be irritable and restless, often ascribes the condition to teething. Weakness of the muscles is noticed, and if the child is of walking age it stops walking and wants to do nothing but lie in bed and rest. Irritability is generally the first symptom to arouse attention. The appetite is soon lost, and this may go on to occasional vomiting. Weight loss begins. Constipation is usual. Rhinitis with excess nasal discharge and excess salivation is often seen. Photophobia develops, pronounced in most cases, but slight in a few, the child remains curled up in bed with its head buried into the pillow away from the light. It cries all day and sleeps very little at night, often for only one or two hours. Sweating may be profuse, the clothing of the child being continually moist. With it may appear the miliarial rash on the body. If the blood pressure is taken it will be found to be elevated, and the pulse rate is raised. The temperature may be normal or slightly elevated. Pulling at the hair is common, and also itching of the skin. It is at this stage that the miserable and pitiful, anxious child develops the classical extremities—pinkness of the hands and feet and sometimes of the face. The "pink" colour, which is due to capillary filling, may show a faint duskiness, which is probably due to cyanosis and can be exacerbated by cold. The hands are cold. The œdema of the hands and feet and rarely of the face (Case XII) is non-pitting. The layers of the skin peel off, becoming more delicate with every successive shedding. Generally desquamation is first noticed between the fingers. So these tender "raw-beef hands and feet" present themselves. Obviously infection readily occurs, and if the circulation becomes too poor ulceration of the extremities develops. In the most severe cases the teeth are shed from their sockets, and ulceration of the mouth with superimposed stomatitis may occur. One child I observed developed gangrene of the whole upper lip with erosion, so that after recovery a plastic operation was necessary.

TABLE I.

Case Number.	Sex.	Age in Months.	Duration of Illness so Far.	Preceding Infection.	Secondary Infection.		Rise in Temperature.	Photophobia.	Anorexia.	Occasional Vomiting.	Condition of Bowels.	Weight Loss.
					Present Earlier.	Present Now.						
I	M.	13	4/12	Cold.	Gastroenteritis.	No.	No.	Yes.	Yes.	No.	Constipated.	Yes.
II	F.	14	2/12	Left *otitis media*.	Bronchopneumonia.	Yes.	To 100° F.	Yes.	Yes.	No.	Normal.	Yes.
III	M.	12	3/12	No.	No.	No.	No.	Yes.	Yes.	No.	Normal.	Yes.
IV	F.	9	6/52	Tracheitis.	Cold.	No.	No.	Yes.	Yes.	Twice.	Constipated.	Yes.
V	F.	21	3/12	No.	Gastroenteritis.	No.	No.	Yes.	Yes.	No.	Constipated.	Yes.
VI	F.	18	2/12	Cold.	No.	No.	No.	Yes.	Yes.	Twice.	Constipated.	Yes.
VII	F.	13	3/12	Cold.	No.	No.	No.	Yes.	Yes.	No.	Normal.	Yes.
VIII	F.	10	3/12	Cold.	Gastroenteritis.	No.	No.	Yes.	Yes.	No.	Normal.	Yes.
IX	M.	6	1/12	No.	Gastroenteritis.	Yes.	To 101° F.	Yes.	Yes.	Yes.	Diarrhœa.	Yes.
X	M.	6	2/12	No.	No.	No.	No.	Yes.	Yes.	No.	Normal.	Yes.
XI	F.	24	3/52	Measles.	No.	No.	No.	Yes.	Mild.	No.	Constipated.	Yes.
XII	M.	7	1/12	*Otitis media*.	No.	No.	No.	Yes.	Yes.	No.	Constipated.	Yes.
XIII	M.	20	2/12	No.	*Otitis media*.	No.	No.	No.	Yes.	No.	Normal.	Yes.
XIV	M.	14	6/52	Bronchitis.	No.	No.	To 99° F.	Yes.	Yes.	Yes.	Normal.	Yes.
XV	F.	9	1/12	*Otitis media*.	Gastroenteritis.	Yes.	To 100° F.	Yes.	Yes.	Yes.	Diarrhœa.	Yes.
XVI	M.	18	2/12	No.	*Otitis media*.	No.	No.	Yes.	Yes.	Yes.	Normal.	Yes.
XVII	M.	10	1/12	Cold.	Bronchopneumonia.	Yes.	To 101° F.	Yes.	Yes.	No.	Constipated.	Yes.
XVIII	F.	66	2/12	Cold.	No.	No.	No.	No.	Yes.	No.	Normal.	Yes.

[1] P, present; A, absent.

The muscle paresis is constant throughout the illness. To feel, the muscles are soft, without any substance. The lymph glands are sometimes enlarged or palpable.

The household is in complete disruption. (The mother loses on an average about two stone in weight from "worry" and lack of sleep, and from hours of strenuous work trying to feed the child.)

A rise in pulse rate and in blood pressure is constantly present, even during sleep. Loss of weight continues, even in those rare cases in which anorexia is not present. In this state severe secondary infection ever hovers near, ready to tip the balance and take the child's life. There are those occasional cases in which suddenly, for no apparent reason, circulatory collapse and hyperpyrexia develop and death follows. As insidiously as they came, so the symptoms generally disappear. Gradually the irritability subsides and the sleep improves. The child begins to take its food. The weight starts to climb, and the first smile appears on the little face. Recovery begins.

In the worst cases, which are not usual, the condition lasts for six to nine months or longer, but usually improvement begins in the third month, as was pointed out by Wood and Wood (1935). One must remember that there are all grades of this condition and some of the signs do not appear; but elevation of the blood pressure, muscle paresis and irritability are constant. In older children the emotional changes are more obvious, and they may complain of headaches. They stop talking or talk infrequently. A reference has been made to *petit mal* attacks and convulsive seizures (extremely rare).

Professor J. C. Spence, in a lecture delivered in Adelaide recently, has drawn attention to the occurrence of bronchiectasis in adults with a history of pink disease in childhood.

Symptomatology of 18 Cases.

The symptomatology of 18 cases has been set out in Table I, at the time when blood was taken for quantitative estimations of the metallic ions in the plasma.

Some Interesting Points Pertaining to These Cases.

CASE XIII.—The mother of this child volunteered the information that the child kept putting his hands into the salt container when at the dinner table, and then putting the salt into his mouth: "He will not take any foods, but he will eat salted peanuts." She wondered whether it would be all right for the child to have salt.

This, I thought, was very interesting and added further evidence to my suspicion. Even wild animals know when they are deficient in salt, and will travel miles to "salt licks".

CASE XI.—A psychological change was shown here. The child showed a dislike for her mother, and persisted in keeping her shoes on when she went to bed at night.

CASE XII.—This boy had severe œdema of the face and scalp, with flaming redness spread across the face and forehead. The œdema of the scalp was non-pitting and soft like a sponge. (This is a rare occurrence. Rocaz (1933) says of this: "In one of my patients, aged eighteen months, the illness began with œdema of the face which was most marked in the eyelids and lips. This symptom has only been reported in a very few cases.") This child went on to a sudden circulatory collapse, with cold cyanosed extremities, vomiting, diarrhœa, temperature of 106° F., and death. *Post mortem*, no secondary infection or gastroenteritis could be detected. No significant findings could be detected on macroscopic examination except an enlarged thymus.

Method of Spectrochemical Determination.

Treatment of the Plasma.—The volume of the plasma was determined in a five millilitre graduated cylinder. It was then transferred to a platinum dish, and the cylinder was washed repeatedly with N/10 hydrochloric acid. Five millilitres of oxalic acid (10%) were added, and the whole was evaporated to dryness on the water-bath. The residue was ignited in front of an open muffle operating at approximately 800° C. The temperature of the interior of the basin was approximately 550° C. It was necessary occasionally to disturb the material in order to obtain a white product. After the basin had cooled, five millilitres of N/10 hydrochloric acid were added, and the basin was warmed for a few seconds on a water-bath to ensure dissolution of the salts. This solution was then stored in a stoppered test tube.

The Determination.—The air-acetylene flame technique of Lundgårdh (1929) for the spectrochemical determination of cations was the method used. This method has been successfully used by Mitchell (1936), Stace (1948) and others, for the determination of these cations in soil extracts and other materials. It is well suited to their determination in plasma. Magnesium and potassium contents were determined by the use of the solution as obtained above. For sodium and calcium a 12·5 fold dilution was necessary. The spectrograph used was a Hilger medium quartz spectrograph with Ilford "Zenith" plates. These were exposed for one minute and developed in a 1:2 metol hydroquinone developer. The opacity measurements were obtained with a Zeiss spectrum line photometer.

Comment.—The method used to obtain these results, as stated, was by spectrophotometry. Marinis, Muirhead, Jones and Hill (1947), using a similar method, found the normal plasma sodium content to lie between 310 and

TABLE I.

Weight Loss.	Psychological Change.	Sweating.	Miliarial Rash.	Hands and Feet.				Redness of Face.	Pulse Rate per Minute.	Blood Pressure. (Systolic/Diastolic, Millilitres of Mercury.)	Hypotonia.	Reflexes.	Rhinitis.	Glandular Enlargement.	Alopecia.	Stomatitis.	Teething Powders Given.
				Redness	Coldness	Œdema	Desquamation										
Yes.	No.	Yes.	Yes.	P[1]	P	P	P	Yes.	180	120/70	Yes.	No, absent.	No.	Yes.	Yes.	No.	Yes.
Yes.	No.	Yes.	No.	P	P	P	P	No.	170	120/80	Yes.	Yes.	No.	No.	No.	No.	No.
Yes.	No.	Yes.	Gone.	P	P	P	P	No.	160	130/90	Yes.	Slight.	No.	No.	Yes.	No.	Yes.
Yes.	No.	Yes.	Gone.	P	P	P	P	Yes.	160	120/80	Yes.	Slight.	Yes.	Yes.	Yes.	Yes.	Yes.
Yes.	No.	Yes.	No.	P	P	P	A[1]	No.	160	120/60	Yes.	Yes.	No.	Yes.	Yes.	No.	Yes.
Yes.	No.	Yes.	Yes.	P	P	P	A	Yes.	160	145/110	Yes.	Yes.	No.	No.	No.	Slight.	Yes.
Yes.	No.	Yes.	Yes.	P	P	P	P	Yes.	180	130/60	Yes.	Slight.	Yes.	Slight.	Yes.	No.	Yes.
Yes.	No.	No.	No.	A	A	A	A	No.	160	120/70	Yes.	No.	No.	Yes.	No.	No.	No.
Yes.	No.	Yes.	Yes.	P	P	P	P	No.	160	110/70	Yes.	Slight.	No.	No.	No.	No.	No.
Yes.	No.	Yes.	Yes.	P	P	P	A	Yes.	170	135/100	Yes.	Slight.	No.	Yes.	No.	No.	Yes.
Yes.	Yes.	Yes.	Yes.	P	P	P	A	No.	150	125/70	Yes.	Slight.	No.	Yes.	No.	No.	No.
Yes.	No.	Yes.	Yes.	P	P	P	P	Yes.	180	150/115	Yes.	Slight.	No.	No.	Yes.	No.	Yes.
Yes.	No.	Yes.	Yes.	P	P	P	P	No.	160	130/100	Yes.	No.	No.	No.	No.	Yes.	Yes.
Yes.	No.	Yes.	Yes.	P	P	P	A	Yes.	150	125/90	Yes.	Slight.	Yes.	Slight.	No.	No.	Yes.
Yes.	No.	No.	No.	P	P	A	A	Yes.	150	95/60	Yes.	Yes.	No.	No.	No.	No.	No.
Yes.	No.	Yes.	No.	P	P	A	A	No.	150	130/90	Yes.	Yes.	No.	No.	No.	No.	Yes.
Yes.	No.	Yes.	Yes.	P	P	P	P	Yes.	180	130/60	Yes.	No.	Yes.	Slight.	No.	No.	No.
Yes.	No.	Yes.	Yes.	P	P	P	P	No.	140	150/100	Yes.	Yes.	Yes.	No.	No.	No.	No.

350 milligrammes *per centum*. Obviously, then, there is in this disease a depression of the plasma sodium level which is not found in unaffected children. The significance of this result can also be appreciated when one realizes that the sodium level in Addison's disease is of the order of 295 milligrammes *per centum*. In fifteen cases out of 16 this depression is found. In regard to Case XVI, the condition was mild and a possible error may have been made in the determination. Results obtained for magnesium and calcium were within normal limits.

TABLE IIA.
Pink Disease.

Case Number.	Sex.	Age. (Months.)	Plasma Sodium Content. (Milligrammes *per Centum*.)	Plasma Potassium Content. (Milligrammes *per Centum*.)
I	M.	13	260	20
II	F.	14	270	19
III	M.	12	260	17
IV	F.	9	280	17
V	F.	21	285	17
VI	F.	18	290	16
VII	F.	13	260	18
VIII	F.	10	290	21
IX	M.	6	270	19
X	M.	6	290	20
XI	F.	24	300	19
XII	M.	7	270	20
XIII	M.	20	280[1]	—
XIV	M.	14	300	19
XV	F.	9	280	17
XVI	M.	18	360	16

Discussion.

This depression of the plasma sodium level is, I believe, a finding of great importance with far-reaching implications, and potentially capable of explaining the symptomatology of this disease and of opening up the way to the cause, pathology and treatment. However, as this is a preliminary paper, no more will be said at this stage except to remark that it would seem apparent from a limited number of cases (three) that the administration of ordinary salt has a beneficial effect.

Blood Pressure.

The blood pressure is significant in this disease. Feer (1923) originally stressed the importance of the rise of systolic pressure, and said it evidenced the dysfunction of the vegetative nervous system. Few writers have taken adequate notice of it, and most have not even mentioned it. Gareau (1942) found that out of his 65 cases, 15 had a systolic blood pressure up to 120 millimetres of mercury. Blood pressures of children, even with this disease, are rarely estimated. It has not been pointed out before that the diastolic pressure is elevated as well as the systolic pressure. Of the series of 18 cases (Table I), an elevation of systolic and diastolic pressures is shown in all and is pronounced in some cases. This phenomenon is constant, and in my opinion is always present and is a valuable diagnostic aid. The rise in diastolic pressure must evidence a widespread increase in peripheral resistance.

TABLE IIB.
Other Children.

Subject Number.	Initials.	Condition.	Age. (Months.)	Plasma Sodium Content. (Milligrammes *per Centum*.)	Plasma Potassium Content. (Milligrammes *per Centum*.)
I	J.W.	Talipes.	7	335	22
II	A.K.	Normal.	9	350	16
III	L.N.	Cut on knee.	24	320	13
IV	W.W.	Normal.	14	335	20
V	G.M.	Cut on forehead.	17	360	14
VI	H.J.	Mastoiditis.	7	320	18
VII	J.B.	Normal.	9	305	14
VIII	Y.N.	Normal.	12	340	16
IX	G.M.	Normal.	17	360	14
X	B.M.	Pneumonia.	6	335	18
XI	J.D.	Recovered from pink disease.	18	315	18
XII	A.L.	Gastroenteritis.	9	360	20
XIII	H.T.	Tuberculosis.	20	340	18
XIV	B.T.	Pneumonia.	10	335[1]	—
XV	C.B.	Coeliac disease.	21	330[1]	—
XVI	J.K.	Gastroenteritis.	6	320[1]	—

[1] These results were obtained by a colorimetric method on the lines and technique of Nylons (described by E. N. Allott, "Recent Advances in Clinical Pathology", First Edition, page 223). Half of the above sodium results were also checked by this method and similar figures were obtained.

The Extremities.

Sir Thomas Lewis (1933*a* and *b*) in his two theses pointed out some very important facts. Although he never mentioned pink disease, he showed that in various diseases, such as acrocyanosis, chilblains, Raynaud's disease, *urticaria factitia* and so-called "erythromelalgia" the skin was in what he called a "susceptible state", or unusually sensitive, if not to pinprick, then to friction and to immersion in water at 40° C. or over. He went on as follows:

> Even temperatures within the normal range of skin temperature may give rise to burning pain from the affected skin and similar pain can be induced at lower temperatures by increasing the tension in the skin as

TABLE III.[1]

Case Number.	Sex.	Age. (Months.)	Erythrocyte Count (per Cubic Millimetre.)	Leucocyte Count (per Cubic Millimetre.)	Differential Leucocyte Count. (Percentages.)					Arneth Count. (Percentages.)					Blood Sugar Level. (Milligrammes *per Centum*.)
					Polymorphonuclear Cells.	Lymphocytes.	Monocytes.	Eosinophile Cells.	Basophile Cells.	One Lobe.	Two Lobes.	Three Lobes.	Four Lobes.	Five Lobes.	
I	M.	13	6,000,000	13,100	60	29	10	—	1	15	60	20	3	2	—
III	M.	12	5,000,000	13,300	63	27	10	—	—	14	60	24	2	—	100
IV	F.	9	5,500,000	12,000	34	44	17	2	3	7	33	41	14	5	—
VI	F.	18	6,100,000	14,000	37	57	4	1	1	26	42	20	10	2	120
X	M.	6	5,100,000	14,500	60	37	2·5	0·5	—	1	13	47	29	10	70
XI	F.	24	4,300,000	12,100	55	32	12	—	1	10	31	39	18	2	80
XII	M.	7	4,200,000	17,700	41	49	9	1	—	3	17	42	28	10	100
XIII	M.	20	6,400,000	13,000	38	53	7	2	—	11	25	35	18	11	—
XIV	M.	14	5,300,000	15,300	41	49	9	1	—	3	17	42	28	10	—
XVI	M.	18	6,000,000	10,500	23	66	9	2	—	34	47	12	7	—	—

[1] No secondary infection was present and these ten children were all afebrile. The cells of the blood are increased in number. This has been pointed out by previous writers. Braithwaite (1936) also found that a rise in the hæmoglobin percentage was a constant feature. The hæmoconcentration has been said to be due to sweating. In some cases a preponderance of polymorphonuclear cells is found, but the Arneth count shows no particular shift either way. The few blood sugar levels estimated (non-fasting) seem a little low.

by venous engorgement or by imposing direct tension upon it. Thus it happens that in the ordinary circumstances of life, skin so affected gives rise to burning pain, particularly when it becomes warm from any cause, when it is rubbed, or, if it is upon the foot when the limb hangs down. The state is, in general, accompanied by redness, and can be produced in normal skin by burning it, freezing it, scratching or by exposure to ultra-violet light.

To explain this feature of a "susceptible state", Lewis put forward the theory, for which he had considerable evidence, that the burning pain and tenderness were due to the liberation of a special substance which acted on the pain nerve endings, and that by rough usage, or merely by circulatory arrest to the part, the concentration of this substance could rise sufficiently to cause continuous burning pain without other interference. He considered that the substance was probably liberated from the cells physiologically, and that when gross damage to cells occurred, or when circulatory arrest took place, the amount of this substance became appreciable.

His group of cases presented various symptoms and signs, complete in some, incomplete in others—namely, burning pain, tenderness, redness, swelling, itching, sweating and coldness (often with a subjective feeling of warmth), also hyperæsthesia and ulceration. Dependency, heat, friction and circulatory arrest increased the burning pain, whereas cold, horizontal posture and immobility gave relief.

Pink disease should be included as one of those diseases which manifest the "susceptible state". These children show redness, coldness, swelling, sweating, itching and hyperæsthesia at some stage or other. Their hands are tender to touch, and they cry out in anticipation when one approaches—afraid of being handled. Further, these children like their hands and feet to be dipped in cool water. Rocaz (1933), in one of his cases, mentions how the child would sit on a tiled floor and rest her bare feet on the cold tiles for hours on end. Conversely it has been mentioned by several writers that these children hate warmth. If tucked up in bed they will immediately throw off their bedclothes. Interestingly enough, mothers have said that they have stopped bathing their children because they scream when taken near the bath, or immediately put their hands and feet straight up out of the water. They do not like a tourniquet placed on their arm, because this further increases their pain from arrest of circulation. The bizarre attitudes which these children assume are governed not only by muscle weakness and photophobia, but partly by the fact that the pain varies with position. May not the photophobia be due to a "susceptible state" of the conjunctiva produced by congestion?

SUMMARY.

1. The history of pink disease and its ætiology and pathology have been reviewed.

2. There is no indication from a study of the literature that a rational basis for therapy exists.

3. Spectrophotometric studies of the plasma of 16 patients suffering from pink disease are presented, together with certain important clinical details. On the basis of the low plasma sodium levels, further research is being conducted into the ultimate cause and rational therapy of the condition. This will be the subject of a further communication at an early date.

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PINK DISEASE OR INFANTILE ACRODYNIA: ITS NATURE, PREVENTION AND CURE.

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IN an introductory paper Cheek and Stace reported the consistent presence of a low plasma sodium level in pink disease or infantile acrodynia, and with the object of following the investigation more intensively the assistance of the physiology department of the University of Adelaide was sought.

The original idea was that a mineral deficiency was the cause of the disease, and the Board of Honoraries of the Adelaide Children's Hospital gave permission to investigate this and, if necessary, to treat the deficiency when found. However, the sweating, raised blood pressure and irritability seemed to indicate a hyperactive sympathoadrenal system, and one of us (D.B.C.) ventured to study this by physiological methods.

To illustrate both the confusion existing on the subject of pink disease and the need for omitting nothing in the way of observation in clinical research, we quote from the monograph of Rocaz (1933): "There is not even a consensus of opinion as to the best name for the malady. On the contrary, it rejoices in a number of names surpassing the claims of most other diseases." The clue to its real cause lay in the chance observation by one of us (D.B.C.) of an extremely swollen face in the terminal stages of a fatal case. This was so unique that he had a photographic record made, and in discussing it with the other author (C.S.H.) he remarked that, though they were swollen, the tissues did not pit on pressure. Cellular turgor resulting from movement of water from the extracellular to the intracellular phase at once suggested itself to C.S.H. as a sequel to low plasma sodium and chloride levels. He (C.S.H.) predicted hæmoconcentration and ascribed the raised diastolic and systolic pressures to this as a hæmodynamic cause; he explained the sweating as being the only remaining effective cooling mechanism, and irritability and photophobia as due to turgor of the cells of the central nervous system. On action being at once taken to test the theory, it was found to apply almost suspiciously well, both as the basis for a diagnostic test and as a guide to treatment by salt administration, with or without desoxycorticosterone acetate, according to the severity of the condition.

The "climate of opinion" plays so prominent a role in encouraging or withering an idea that it is worth placing on record that in his Listerian Oration of May 28, 1930, Hicks surveyed in detail the evidence for vegetative regulation of the body as illustrated by the response to nonspecific therapy. He made a plea for examining disease more from the standpoint of Claude Bernard's *"milieu intérieur"* than from that of morbid anatomy.

If one examines the voluminous literature on pink disease and studies the painstaking work done to follow the logic of organ pathology and infection, it becomes clear that Claude Bernard was like unto the "pelican in the wilderness or the owl in the desert", so little has been the part played by physiological thinking.

Vipond in 1922, for example, used an autogenous vaccine from tonsillar organisms with apparent success, and Rodda (1925) and later Gareau (1942), who records a large series, ascribed his excellent results to removal of infected

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TABLE I.
Blood Findings Before Treatment.

Patient.	Age.	Plasma Sodium Content.[1]	Cell Volume *per Centum.*[2]	Hæmoglobin Value. (Grammes *per Centum.*)[3]	Plasma Protein Content. (Grammes *per Centum.*)	Non-fasting Blood Sugar Level. (Milligrammes *per Centum.*)	Blood Pressure. (Systolic/Diastolic, Millimetres of Mercury.)	Pulse Rate per Minute.	Urinary Chloride Content. (Grammes *per Centum.*)
Dianne B. ..	9 months.	300	45	14·6	6·9	90	110/80	140	1·3
Graham A. ..	1 year 3 months.	280	43	15·0	7·7	110	130/90	140	0·7
Richard P. ..	6 months.	280	51	16·1	5·6	110	120/90	150	0·8
Maureen C. ..	1 year.	300	42	13·5	8·1	80	100/70	130	0·7
Perry G. ..	9 months.	280	48	14·8	7·5	80	130/80	150	0·5
Leone B. ..	10 months.	300	42	13·8	7·3	100	120/70	150	1·2
Paul B. ..	6 months.	290	41	13·8	6·7	100	110/80	150	1·5
Gillian C. ..	2 years 3 months.	295	48	15·3	8·1	80	110/80	110	1·0
Christine B. ..	1 year 7 months.	280	52	17·0	7·5	130	120/70	150	1·8
Peter M. ..	8 months.	280	46	15·3	7·8	130	130/90	150	1·2
Carol D. ..	1 year.	280	45	15·3	7·4	100	110/80	180	1·6
Ian C.	7 months.	280	44	14·6	6·6	80	130/100	180	1·6
Dennis C. ..	1 year 2 months.	250	45	16·1	7·1	80	130/100	200	1·2
Anne D. ..	4 years.	300	44	13·9	7·7	100	100/60	110	0·6

[1] Normal, 310 to 360 milligrammes *per centum.*
[2] Normal, 35±5.
[3] Normal, 11.

tonsils. All these effects could reasonably be ascribed to a non-specific response to tissue trauma on the part of the vegetative mechanism, of which the sympatho-adrenal system forms the most sensitive reactor to changes in external and internal environment.

As soon as it was reasonably certain that investigations along the line of suprarenal hypofunction might prove fruitful, an appeal was made by circular letter through the British Medical Association for cooperation by practitioners with cases of pink disease.

Patients were either concentrated in the clinic of Dr. F. N. LeMessurier at Mareeba Babies' Hospital or studied in their homes. We are particularly indebted to Dr. LeMessurier for his prompt assistance and his clinical assessment of patients in his care.

Evidence will be adduced to support the view that the phenomena of pink disease are due to a water-salt imbalance leading to anhydræmia with a tendency to cellular turgor. Underlying this water-salt imbalance is a hypofunction of the suprarenal gland—in our opinion both cortex and medulla are involved—with a lowered renal salt threshold and disordered glucose metabolism. In the late stages of a severe case disordered absorption of glucose occurs, together with diarrhœa, rapid increase of anhydræmia, hæmoconcentration, and death from vascular shock.

As concomitants of the increasing ill-being are lowered food intake and hypoproteinæmia, which further aggravate the water imbalance and the severity of the diarrhœa.

It is remarkable that the evidence of hæmoconcentration in the form of polycythæmia and leucocytosis should have been so long missed, doubtless owing to the association of the latter with response to infection.

CLINICAL AND LABORATORY INVESTIGATION.

In the preliminary paper the constant finding of a low plasma sodium level and high blood pressures was recorded in 16 cases. In the present series the same data are presented, together with the evidence for the presence of hæmoconcentration. Detailed investigations of urinary volume and chloride content as well as of carbohydrate metabolism were not conducted. Some evidence on these aspects is presented in cases in which it was readily obtainable.

It is obvious from inspection of Table I that a pronounced hæmoconcentration is characteristic of the present series, and it is not too much to infer that the previously reported series differed in no way from this so far as hæmoconcentration is concerned.

It is reasonable to suppose that the leucocytosis is a result of this hæmoconcentration, as are doubtless the high values found for plasma protein content. However, strict proportionality between cell volume and percentage of plasma protein does not appear to be the case, possibly because high concentrations are balanced by altered rates of formation. Low values, on the other hand, occur where there is clinical evidence of low food intake for some time previously, and the true values are no doubt lower still. Whether, as in the case of Richard P., they are as low as $5{\cdot}6 \times \frac{35}{51} = 3{\cdot}5$, we cannot accurately determine, but from the effect of intravenous plasma administration in the same case it is a fair inference that the percentage of plasma protein must have been very close to this figure.

In the case of electrolytes the renal threshold will be the main factor in determining the blood levels. The glucose levels, however, indicate some alteration of carbo-

TABLE II.
Blood Findings After Treatment.

Patient.	Age.	Plasma Sodium Content.	Cell Volume. (*Per Centum.*)	Hæmoglobin Value. (Grammes *per Centum.*)	Non-fasting Blood Sugar Level. (Milligrammes *per Centum.*)	Plasma Protein. (Grammes *per Centum.*)
Dianne B.	9 months.	400	38	12·5	100	6·3
Jeffrey G.	8 months.	330	38	12·4	110	7·2
Richard P.	6 months.	320	38	12·0	80	6·4
Maureen C.	1 year.	320	38	12·5	80	7·8
Leone B.—						
(i)	10 months.	325	38	12·3	70	7·2
(ii)		315	38	12·3	100	7·0
Paul B.	6 months.	335	39	12·8	100	6·5
Gillian C.	2 years 3 months.	360	34	11·8	90	6·4
Carol D.	1 year.	390	39	12·8	70	6·2
Ian C.	7 months.	360	37	12·4	80	6·2
Dennis C.	1 year 2 months.	330	36	11·3	80	6·7
Anne D.	4 years.	330	38	13·0	80	7·0

hydrate metabolism, and though non-fasting values are given, it will be evident that they are in some cases lower than the fasting level. Changes produced by the correction of hæmoconcentration give support to this conclusion, and there is the possibility that administration of desoxycorticosterone acetate has a direct influence on carbohydrate metabolism. The one case in which it was possible to estimate the rate of glucose absorption shows this to be defective.

When estimations of urinary chlorides were made it appeared that these were high at the early stages of the disease and lower as the condition progressed. Gillian C., for example, in a 24-hour output of 325 millilitres, passed 3·5 grammes of sodium chloride at a time when her plasma sodium content was as low as 295 milligrammes *per centum*.

Further and detailed investigation of this aspect of the salt-water balance should prove illuminating; but the disclosure of a certain means to therapeutic relief puts an ethical limit to the extent to which further experimentation is justifiable at this juncture. There is the known and significant relation to this of the large salt reserve of the infant, as well as a possibly low rate of alimentary absorption due to suprarenal hypofunction (*vide* Stein and Wertheimer, 1941).

Symptomatology.

Briefly, there occurs first and insidiously an abnormal loss of salt owing to the lowered renal threshold for sodium. This loss must cause a variable influence upon the salt-water balance owing to the effect of salt reserves, concerning the nature of which we are as yet not well informed. Water is lost with the salt, and thirst leads to its replacement without salt. The result is a lowering of sodium and chlorine ions in the extracellular water of the body, which includes blood and interstitial fluid. The lowered electrolytic osmotic pressure of the extracellular fluid leads to passage of water into the cells, with consequent swelling as a major effect. There occur thus a loss of water from the blood and concentration of its cytological elements, rise of viscosity, lowering of blood volume and consequent raised systolic and diastolic blood pressures and pulse rate.

Report of Cases.

Case I.—Maureen C., aged two years, had been ill for two months. (This child was fully referred to in the preliminary report and comment was made on her psychological change, in that she showed dislike for her mother and persisted in keeping her shoes on at night.) She screamed if taken near a hot bath. At the stage at which treatment was started, she was eating and sleeping poorly, and the mother stated that the child had no energy and would run around for only a short time each day. She still showed a dislike for the light, but this had improved from what it had been. Sweating was slight and also the pinkness of her hands. She had not gained in weight. Irritability was still present, but the psychological changes were less.

The blood findings were as follows: the plasma sodium content was 300 milligrammes *per centum*, the cell volume was 42%, the plasma protein content was 8·1 grammes *per centum*, the hæmoglobin value was 13·5 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The systolic blood pressure was 100 millimetres of mercury and the diastolic pressure 70 millimetres; the pulse rate was 130 per minute.

The child was given one to two teaspoonfuls of ordinary salt, added to her diet daily. She did not refuse the salt at all. After ten days' treatment with salt the tone of the muscles improved—they felt firm again; the child ran around for most of the day without becoming unduly tired. She ate and slept normally, no irritability was present, she smiled and laughed, and she had gained one pound in weight. At this stage the blood findings were as follows: the plasma sodium content was 320 milligrammes *per centum*, the cell volume was 38%, the plasma protein content was 7·8 grammes *per centum*, the hæmoglobin value was 12·5 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The systolic blood pressure was 90 millimetres of mercury and the diastolic pressure was 50; the pulse rate was 110 per minute. This reversal of symptoms was maintained.

The patient in this case was a child, aged two years, who had been suffering from this disease for two months and who presented photophobia, irritability, insomnia, anorexia, lassitude, muscle weakness, stationary weight, slight sweating and slight psychological change, mild pinkness and some coldness of the hands. She was treated by the addition of one to two teaspoonfuls of salt per day to her diet; the result was the disappearance of her symptoms, a fall in hæmoconcentration, a rise in plasma sodium content, and a fall in blood pressure. It is our impression that this child was not severely affected and was coming to the end of her illness and that the administration of salt quickly made up her deficit, thus producing a rapid reversal of symptoms.

Case II.—Graham A., aged fourteen months, when examined had a history, extending over two months, of slight photophobia, pronounced irritability, sleeplessness, poor appetite, and vomiting regularly once per day after his midday meal. He had had a rash one month previously. His muscle weakness was severe, he had no energy, and he was extremely miserable with dark shadows under his eyes; his hands and feet were red, cold and œdematous. His pulse rate was 150 per minute, and his blood pressure was 125 millimetres of mercury, systolic, and 90 millimetres, diastolic. His appearance was one of exhaustion, and the child lay listlessly in bed. The sister in charge was of the opinion that the child would die.

The administration of salt by mouth was started, one to two teaspoonfuls being given daily, and after three days' treatment the sister of the ward reported improvement. The child began to eat and sleep better, his irritability became less and he began to sit up and play with toys. He smiled occasionally. His weight still remained stationary, and his hands and feet were still the same. This child was maintained on salt treatment alone. His eating and sleeping were improved, and his irritability was less. After twelve days' salt treatment the blood findings were as follows: the plasma sodium content was 280 milligrammes *per centum*, the cell volume was 43%, the hæmoglobin value was 15 grammes *per centum*, the plasma protein content was 7·7 grammes *per centum*, and the non-fasting blood sugar level was 110 milligrammes *per centum*. The blood pressure was 120 millimetres of mercury, systolic, and 70 millimetres, diastolic; the pulse rate was 150 per minute. After a further two weeks' salt treatment the child started to gain weight.

This was a severe case of two months' duration. The administration of salt alone by mouth did not, over a period of a month, completely relieve the condition. The salt alone relieved the irritability, anorexia and lassitude. The hands and feet were unaffected. There was a weight gain only after a month's treatment; after a further month of salt treatment recovery was complete.

Case III.—Perry G., aged nine months, had been ill for six weeks. When this child was examined he exhibited severe photophobia, irritability, anorexia, sleeplessness, hyperhidrosis, typical red, swollen and cold extremities, muscle weakness, a sudaminal rash over the chest and back, and constipation. The blood findings were as follows: the plasma sodium content was 280 milligrammes *per centum*, the cell volume was 48%, the hæmoglobin value was 14·8 grammes *per centum*, the plasma protein content was 7·5 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The blood pressure was 130 millimetres of mercury, systolic, and 80 millimetres, diastolic; the pulse rate was 150 per minute.

One to two teaspoonfuls of salt were added to the milk and food daily. After eighteen days' treatment most symptoms had been lost. The muscles were firm; the mother said the child was active. He was eating and sleeping well, but his weight still remained stationary. The child smiled; the hands were no longer pink or cold, and the mother said that only strong light now worried the child. After a further week the child displayed no symptoms, and he had gained half a pound in weight. His blood pressure was 100 millimetres of mercury, systolic, and 60 millimetres, diastolic, and his pulse rate was 120 per minute.

This child had an illness of six weeks' duration, which was treated with salt with a reversal of symptoms in three weeks.

Case IV.—Peter M., aged eight months, had been ill for one month. The mother had noticed that the child was not eating and had become irritable. Sleep was becoming unsatisfactory. For the last three weeks prior to his admission to hospital the child had been sweating and had shown a dislike for the light. Pinkness, coldness and swelling of the hands and feet developed.

Examination of the child revealed soft muscles, pink, cold, swollen hands and feet, palpable lymph glands and moist skin. The blood findings were as follows: the plasma sodium content was 280 milligrammes *per centum*, the cell volume was 46%, the hæmoglobin value was 15·3 grammes *per centum*, the plasma protein content was 7·8 grammes *per centum*, and the non-fasting blood sugar level was 130 milligrammes *per centum*. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure 90; the pulse rate was 150 per minute.

The child was given salt, one to two teaspoonfuls daily. After two weeks the mother reported that irritability was only slight, and that on some nights the child woke once or twice, but that on other nights he slept right through. No sedation was required. His appetite was fair. The hands and feet were unaltered. The blood findings were as follows: the plasma sodium content was 290 milligrammes *per centum*, the cell volume was 44%, the hæmoglobin value was 13·2 grammes *per centum*, the plasma protein content was 7·2 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure 90. The pulse rate was 150 per minute.

The child was then given whole suprarenal gland, three grammes daily, in a powdered form with the food for a further two weeks. At the end of this period no further improvement had been made, except for the mother's impression that the child was more bright and alert, and that the pinkness of the hands was less obvious. She said that the child was quite happy, laughing and smiling often during the day, and no source of worry to her whilst she did her work. On cessation of the suprarenal gland treatment, the redness of the hands did seem to become more prominent. The child continued to be happy and contented, eating and sleeping well.

This child received salt alone for fourteen days and an amelioration of symptoms occurred. On the administration of whole suprarenal gland as well as salt for another fourteen days some further improvement was noticed; but this, we believe, was due to the salt alone rather than to the whole suprarenal gland extract.

CASE V.—Gillian C. was aged two years and three months. Eight months earlier the mother had noticed that the child was beginning to sweat, that she was restless at night and that she would not eat her food. The child developed a rash, and the mother was told by her doctor that it was "allergic". The rash persisted for several days. A month later the child lost a lot of hair and her weight remained stationary. Constipation was noticeable. The mother consulted several doctors and in each instance was told that "teething was the trouble". Three months later again another rash appeared, and this time a diagnosis of measles was made. Restlessness and irritability continued and a psychological change became manifest—the child flew into rages, kicked and hit her mother and threw things at her. "Previously she had always been an affectionate and timid child." Teething was again blamed for the condition. During the last three months the mother had noticed the child had no energy: "She just wants to sit all day in her little chair. Sometimes if she gets up to walk she falls over, just as if her legs give way." The mother said that her sleep was still poor. Her weight, which had been stationary for six months, now was falling. She had lost three pounds in the last month. During this time she had been admitted to hospital for treatment of cervical adenitis. This had subsided, and she had been discharged from the out-patient department with a tonic.

It was noticed at the out-patient department by one of the nurses that the hands of this child were peeling. At that stage the child came under our notice. The light had never worried her unduly except recently when she went to bed at nights; she would say to her mother: "No light." When this child was examined she was eating and sleeping poorly and subject to psychological outbursts. She remained seated in her chair all day long, speaking as seldom as possible. At no stage had there been any suspicion of pinkness of the hands or feet, but the mother stated that the hands were often cold and moist, and that in the last two weeks they had been peeling. "Early in the year the child had passed a lot of water, but now it seemed rather scanty." The blood findings were as follows: the plasma sodium content was 295 milligrammes *per centum*, the cell volume was 48%, the hæmoglobin value was 15·3 grammes *per centum*, the plasma protein content was 8·1 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The blood pressure was 110 millimetres of mercury, systolic, and 80 millimetres, diastolic; the pulse rate was 110 per minute. A twenty-four hours' specimen of urine (volume 325 millilitres) contained 3·3 grammes of chloride (expressed as sodium chloride). The blood chloride content equalled 425 milligrammes *per centum* (expressed as sodium chloride) at the time when the first specimen of urine was collected. After the administration of two teaspoonfuls of salt, the volume of the next twenty-four hours' specimen of urine was 783 millilitres, and it contained 9·4 grammes of chloride (expressed as sodium chloride).

Salt—one to two teaspoonfuls per day—was given. Five days later the mother noticed that the child was beginning to get up and move around more, and that on the fifth night after treatment she slept soundly for the whole night—the first time for eight months. (The mother had been getting up to this child two and three times a night for one or two hours for the past eight months.) At this stage powdered whole suprarenal gland was administered (this was freshly prepared from abattoir steers). It was given by mouth with the food in amounts of about one gramme daily. On the eighth day after salt treatment was begun a remarkable change occurred. The little patient was bright-eyed and alert, with much more energy and rosy cheeks—she pointed to things around the house and talked continuously. The mother reported that she was even sleeping during the day, and that she wanted to rest in her chair for only two to three hours each day. Two days later the mother reported that the child was playing and running around most of the day, sleeping satisfactorily and talking normally, that she was interested in her surroundings, but that food was still taken with persuasion. Thirteen days after treatment was begun, the mother described the child as a "live-wire"; she said that she was full of energy, but that the appetite was still poor, in that the child had to be coaxed a great deal to take her food. There had been a gain of two pounds in weight.

On the sixteenth day four milligrammes of desoxycorticosterone acetate were given daily. Three days later the mother reported an improvement of the appetite. The blood findings at this stage were as follows: the plasma sodium content was 360 milligrammes *per centum*, the cell volume was 34%, the hæmoglobin value was 11·8 grammes *per centum*, the plasma protein content was 6·4 grammes *per centum*, and the non-fasting blood sugar level was 90 milligrammes *per centum*. The systolic blood pressure was 90 millimetres of mercury and the diastolic pressure was 60 millimetres; the pulse rate was 100 per minute.

Injections were given three times a week for two weeks, and the child remained well and happy, and continued to gain weight. However, the high salt intake was continued.

This child had been ill for eight months and had been examined by seven different doctors during the course of her illness, and in each instance the diagnosis had been missed. We believe that this is due to the fact that the diagnosis of pink disease is too closely associated with pink hands and photophobia. The name pink disease or erythrœdema is really a misleading one.

The symptoms of this child—the lassitude, the muscle weakness, the irritability, the sleeplessness, the inertia and the failure to gain in weight—were reversed by the administration of ordinary salt. We are of the opinion that the suprarenal gland played little part in this, because we found later with other children that it was ineffective by itself.

The fact that this child would literally sit all day brought to mind the observations of McCance (1936) and his colleagues, when they experimentally depleted themselves of salt. McCance found that exertion was a considerable effort and that his colleagues just wanted to sit all day. McCance also reported inability to taste salt, as apparently is the case with these children.

Although this child gained in weight, salt alone did not restore a healthy appetite, although she would take her food with persuasion. The injections of desoxycorticosterone acetate improved the appetite.

CASE VI.—Dianne B., aged nine months, had been irritable and losing weight and having profuse night sweats for the last six weeks. Recently her hands and feet became pink and cold and she burrowed her head into the pillow and bedclothes. At the time of examination she had a rash on chest, back and thighs. She was difficult to feed and constipated. She vomited occasionally. Her muscles were soft, and she scarcely slept at night.

On examination of the patient, the muscles were flaccid. A sudaminal rash was present on the chest and back. Redness, coldness and swelling of the hands and feet were present. The blood findings were as follows: the plasma

sodium content was 300 milligrammes *per centum*, the cell volume was 45%, the hæmoglobin value was 14 grammes *per centum*, the plasma protein content was 6·9 grammes *per centum*, and the non-fasting blood sugar level was 90 milligrammes *per centum*. The systolic blood pressure was 110 millimetres of mercury and the diastolic pressure 80 millimetres; the pulse rate was 180 per minute.

Salt administration—one to two teaspoonfuls per day—was begun, and intramuscular injections of desoxycorticosterone acetate were started on the fourth day, two milligrammes being given daily for four days, then four milligrammes daily for the next four days.

Five days after treatment was begun, photophobia, irritability and the sweat rash disappeared. By the ninth day sweating was slight and the child was eating and sleeping well. No sedation was necessary. By the eleventh day the child was picking up and playing with toys and was bright-eyed and talking. The honorary pædiatrician was impressed with the good improvement. The blood findings were as follows: the plasma sodium content was 400 milligrammes *per centum*, the cell volume was 38%, the hæmoglobin value was 12·5 grammes *per centum*, the plasma protein content was 6·3 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*. The systolic blood pressure was 110 millimetres of mercury and the diastolic pressure was 80; the pulse rate was 150 per minute.

On the thirteenth day the child had lost all obvious symptoms of the disease except that a slight pinkness of the hands persisted, but they were warm. Sometimes this pinkness was not at all noticeable. At this stage the desoxycorticosterone acetate injections were stopped to see if this reversal of symptoms could be maintained on salt alone. However, it was then noticed that there was a small abscess forming on the thigh from an infected pimple. This caused the child to be a little irritable, but she still slept without sedation. On the eighteenth day the abscess discharged, and from the eighteenth to the twenty-second day the child was apparently well and happy, eating and sleeping well, with occasional faint pinkness of the hands, which were generally warm.

On the twenty-second day the salt treatment was stopped. Five days after this, the sister in charge of the ward reported that the child had vomited after feeds, that some irritability had returned, that the child was whimpering frequently, and that she was "burrowing". Six ounces in weight had been lost. The sister's impression was that the child's condition had regressed, and that eating and sleeping were now only fair. This also was the opinion of the doctor in whose care the child was. The blood findings at this stage were as follows: the plasma sodium content was 290 milligrammes *per centum*, the cell volume was 47%, the hæmoglobin value was 14·6 grammes *per centum*, the plasma protein content was seven grammes *per centum*, and the non-fasting blood sugar level was 60 milligrammes *per centum*. The systolic blood pressure was 125 millimetres of mercury and the diastolic pressure was 80; the pulse rate was 150 per minute.

At this stage, unfortunately, it was necessary for the child to be sent home. The parents were of the opinion that her condition was much improved from when she went into hospital; but as the days went by, feeding became less easy, sleep poor, irritability more noticeable, and the child developed another boil on the thigh. The administration of salt per mouth was again started, and the condition of the child then began to improve. She became less irritable, crawling about and smiling. The child seemed much improved after the abscess had discharged. The mother reported a gain of half a pound in weight after a week's treatment with salt. In the following week the child lost all obvious symptoms of the disease.

The symptoms of this child were relieved by the administration of salt and the intramuscular injection of desoxycorticosterone acetate. On the cessation of the injections it seemed that the improvement was maintained, but the development of an abscess on the thigh complicates evaluation of the treatment. It is reasonable to assume that this would cause the child to be somewhat irritable. The child was quite happy after this first abscess had discharged. On the cessation of salt intake there were a gradual return of symptoms and a loss of weight, and the hæmoconcentration which had been reduced once more returned. The child's condition declined also when she was sent home, but here again another abscess complicated the picture. After this had discharged and salt had been given by mouth there occurred a gradual disappearance of the symptoms, a gain in weight, and uninterrupted recovery.

CASE VII.—Leone B., aged ten months, had had an infective cold two months earlier, and then developed a rash and profuse nasal discharge. She became irritable and showed a dislike for the light. She had had frequent night sweats during the past fourteen days, and one week prior to her admission to hospital her feet and hands became pink and cold. She was difficult to feed and occasionally vomited. Her stools were relaxed and her sleep was poor. Heavy sedation was necessary. The child would not sit up, and the muscles were weak.

On examination, the child had typical red, cold extremities, flaccid muscles and obvious photophobia, and was sweating. Nasal discharge was obvious and she was seen to rub her hands together. The blood findings were as follows: the plasma sodium content was 300 milligrammes *per centum*, the cell volume was 42%, the hæmoglobin value was 13·8 grammes *per centum*, the plasma protein content was 6·7 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*. The systolic blood pressure was 120 millimetres of mercury and the diastolic pressure 70 millimetres; the pulse rate was 150 per minute.

This child was observed for three days in hospital, so as to confirm the mother's story. On the fourth day the intramuscular injection of desoxycorticosterone acetate, four milligrammes daily, was started, together with the administration of one teaspoonful of salt with the food. On the seventh day sedation was found to be unnecessary and was stopped. The child took her food readily and irritability disappeared. Sleep was satisfactory.

By the ninth day after her admission to hospital (fifth day of treatment) the sweating had subsided, and the baby was eating and sleeping as a normal child. There was no nasal discharge, the extremities were normal and warm, and she had gained half a pound in weight. The honorary pædiatrician noted this improvement. On the ninth day of treatment the blood findings were as follows: the plasma sodium content was 325 milligrammes *per centum*, the cell volume was 38%, the hæmoglobin value was 12·3 grammes *per centum*, the plasma protein content was 7·2 grammes *per centum*, and the non-fasting blood sugar level was 70 milligrammes *per centum*. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure was 90 millimetres; the pulse rate was 140 per minute.

The desoxycorticosterone acetate injections were then given on alternate days for four days. The weather during this period was rather hot, and the child redeveloped some degree of irritability; the nurse reported that she took her feeds less readily. There was a slight loss in weight. The irritability and decrease in appetite disappeared on reversion to daily injections of four milligrammes of desoxycorticosterone acetate. This condition was maintained, the only feature being some slight pinkness of the hands, which were generally warm. A week after the reintroduction of the daily injections, the blood findings were as follows: the plasma sodium content was 315 milligrammes *per centum*, the cell volume was 38%, the hæmoglobin value was 12·3 grammes *per centum*, the plasma protein content was 7·0 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*. The systolic blood pressure was 110 millimetres of mercury and the diastolic pressure was 60 millimetres; the pulse rate was 130 per minute.

The child remained well with no symptoms after three weeks' treatment. The injections were stopped and the child remained well on salt treatment alone.

Six days of treatment with salt and desoxycorticosterone acetate (four milligrammes per day) abolished the symptoms except for a slight pinkness of the hands. There was a slight return of irritability and difficulty with feeding when the injections were reduced to alternate days. The hot weather may have been responsible for this. However, the symptoms disappeared on reestablishment of the daily injections. After three weeks of injections these were stopped and the patient remained well on salt treatment alone.

CASE VIII.—Christine B., aged one year and seven months, had a history of three weeks' illness beginning with a cold. The child was miserable and irritable, crying all day long and refusing food. Her sleep was poor—she was awake most of the night. She was sweating profusely and very thirsty. Here hands and feet were pink and cold. Constipation had been present for two weeks, and a generalized rash for the last three days. She had a nasal discharge, and her weight was stationary.

On examination, the child was seen to be extremely irritable and hostile. A sudaminal rash covered her chest and back. Her hands and feet were red, cold and swollen and her muscle tone was poor. The blood findings were as follows: the plasma sodium content was 280 milligrammes *per centum*, the cell volume was 52%, the hæmoglobin value was 17 grammes *per centum*, the plasma protein content was 7·5 grammes *per centum*, and the non-fasting blood sugar level was 130 milligrammes *per centum*. The systolic blood pressure was 120 millimetres of mercury and the diastolic pressure was 70 millimetres; the pulse rate was 150 per minute.

The child was given four milligrammes of desoxycorticosterone acetate intramuscularly per day, and one teaspoonful of salt with the food. One week after treatment began the sweat rash had almost disappeared and sweating had stopped. There was no irritability, and the child was happy playing with her toys, and talking and smiling frequently. She had been sleeping normally from the fifth night, no sedation of any kind being used; she ate as a normal child. Her hands and feet were still a little pink and cold. The honorary pædiatrician was surprised at the improvement, because in his opinion this child was severely affected, and in the normal course of circumstances would, at this stage, have been expected to be deteriorating rapidly. Muscle tone gradually improved, and the little patient began to stand up on her bed, and two days later she began to walk around a little.

Having satisfied ourselves that this improvement was maintained, we waited until the eleventh day, and then replaced the desoxycorticosterone acetate with whole suprarenal gland, two grammes being given by mouth daily. At this stage she had shown a gain of four ounces in weight. After a week's treatment along these lines we noticed a slight retrogression in her condition. She still was eating and sleeping well, and playing during the day, but the heavy look returned to her eyes and she was sweating a little. She did not seem quite so happy, and she had lost half a pound in weight. Desoxycorticosterone acetate treatment was resumed, and after a further four days she was bright and happy again, walking and talking, smiling, and eating and sleeping well, and she had gained six ounces in weight. Her hands were sometimes normal in colour and warm, but at odd times during the day a slight pinkness and coldness could be detected.

At the request of the honorary pædiatrician all treatment was now stopped. Forty-eight hours later the blood findings were as follows: the plasma sodium content was 310 milligrammes *per centum*, the cell volume was 44%, the hæmoglobin value was 14 grammes *per centum*, the plasma protein content was 7·1 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The systolic blood pressure was 120 millimetres of mercury and the diastolic pressure was 70 millimetres; the pulse rate was 150 per minute.

Four days after treatment was stopped, another—and a more pronounced—deterioration of the child's condition was obvious. She refused food, had to be forcibly fed and vomited afterwards. She was more irritable, pinkness and coldness of the hands returned, and sleep became unsatisfactory. She began to lose weight. After a week, treatment was resumed, and as quickly as the symptoms had reappeared they once more disappeared. Five days of salt and desoxycorticosterone acetate treatment made the child once more symptom free and induced a rapid gain in weight.

This was a case in which all the symptoms and signs of pink disease were present—an early case of three weeks' history, and thought by outside opinion to be a severe case; in a week the patient showed dramatic improvement and a cessation of symptoms. When the steroid was replaced by whole suprarenal gland this improvement was not maintained. We therefore realized that whole suprarenal gland was not effective, at all events in the dosage used (two grammes daily). On reversion to the steroid injections improvement again was obvious, and when her condition was satisfactory all treatment, salt and steroid, was stopped. This again led, but much more obviously, to a return of the symptoms, which readily disappeared on the resumption of treatment. It thus became apparent that we could make this group of symptoms and signs reappear or disappear at will by treatment or the withholding of treatment. The fluctuations of weight with and without treatment are shown in Figure I.

CASE IX.—Dennis C., aged fourteen months, had been well until three weeks prior to examination, when he developed a cold, and since then he had been miserable and irritable, crying all the time. He did not like the light and burrowed into the pillow. His appetite was lost and his sleep was poor—he awoke every hour during the night. He had a rash all over his body and sweated profusely.

On examination, the patient was found to have a rash front and back, muscle paresis and a moist skin. He was an extremely miserable child, with cold, swollen, pink hands. The blood findings were as follows: the plasma sodium content was 250 milligrammes *per centum*, the cell volume was 45%, the hæmoglobin value was 16 grammes *per centum*, the plasma protein content was 7·1 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure was 100; the pulse rate was 200 per minute. The blood sugar curve before treatment was as shown in Figure II. (Eight grammes of glucose were administered orally and the venous blood sugar content was determined. The child's weight was 21·5 pounds.)

The child was kept in hospital for four days to verify the mother's story, which was found to be correct, except that the child was eating a little better than she had stated. At this stage treatment was commenced; one teaspoonful of salt was given by mouth, and steroid (four milligrammes per day) was given by intramuscular injections daily. Six ounces in weight were lost in the child's first four days in hospital, but two days after the commencement of treatment, this amount was replaced. After three days' treatment the child was less irritable, using his muscles and sleeping and eating well.

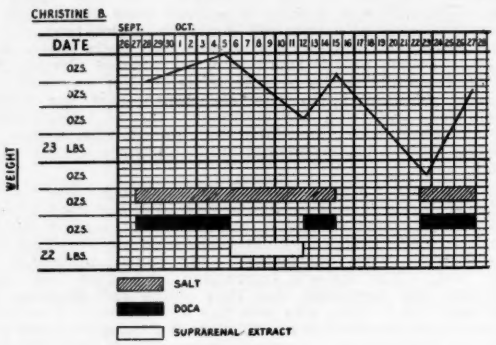

FIGURE I.

Case VIII: Fluctuations of weight with and without treatment.

After ten days of treatment, the condition was satisfactory—he was eating and sleeping well, but was still irritable at times during the day. Photophobia had disappeared. The dosage of steroid was then increased to six milligrammes per day, and the salt intake was increased to two teaspoonfuls by mouth. Four days later the child was well and happy. Some slight pinkness of the hands was still present, although they were warm. The blood findings at this stage were as follows: the plasma sodium content was 330 milligrammes *per centum*, the cell volume was 36%, the hæmoglobin value was 11·3 grammes *per centum*, the plasma protein content was 6·7 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The blood sugar curve at this stage, after treatment, was as shown in Figure III.

This child, as can be seen from the blood findings, was severely affected and more energetic treatment was required.

CASE X.—Carol D., aged twelve months, had been ill for three weeks. The mother had consulted an eye specialist because of the child's severe photophobia. There had been a loss of appetite and weight, and occasional vomiting over the last three weeks. The child was miserable and irritable and sleeping poorly. The mother had noticed a generalized rash two weeks earlier, and sweating was also present. The child had been constipated over the last two weeks.

On examination of the patient, the muscles felt flaccid. Pinkness of the hands and feet had not yet developed, but they were cold and moist. The lymph glands were enlarged. The blood findings were as follows: the plasma sodium content was 280 milligrammes *per centum*, the cell volume was 45%, the hæmoglobin value was 15·3 grammes *per*

centum, the plasma protein content was 7·4 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*. The systolic blood pressure was 110 millimetres of mercury and the diastolic pressure was 80; the pulse rate was 180 per minute.

The child was given salt, one to two teaspoonfuls by mouth for the first three days. No improvement was apparent. Injections of steroid, four milligrammes daily, were then given. After the sixth injection the mother reported that the child was eating and sleeping well, waking only once or twice during the night. The child was walking about and not sweating; photophobia was still present, but was now noticeable only in the strong sunlight. The hands and feet were warm. The blood findings at this stage were as follows: the plasma sodium content was 390 milligrammes *per centum*, the cell volume was 39%, the hæmoglobin value was 12·8 grammes *per centum*, the plasma protein content was 6·2 grammes *per centum*, and the non-fasting blood sugar level was 70 milligrammes *per centum*.

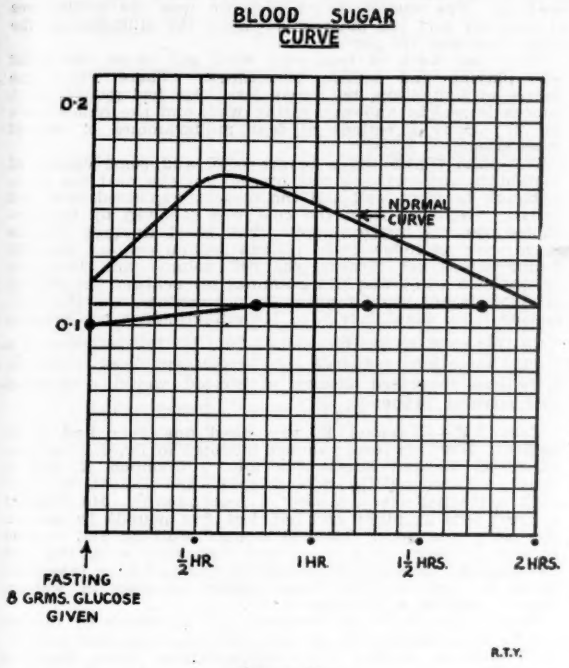

FIGURE II.

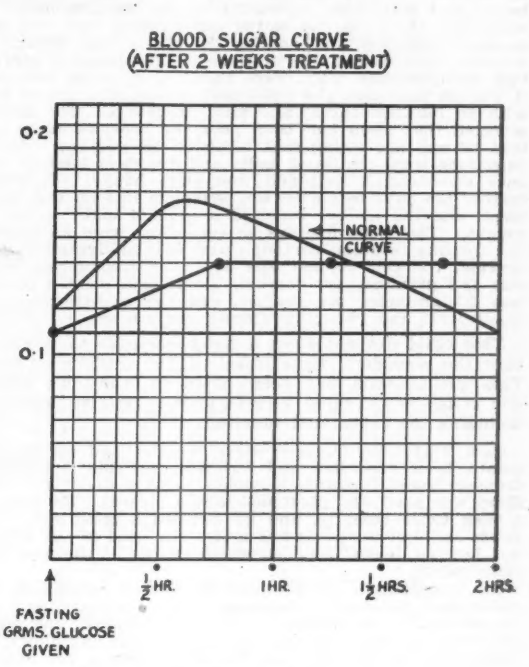

FIGURE III.

Figures II and III: These blood sugar curves from Case IX serve to indicate the retardation in carbohydrate absorption and metabolism, suggested by the non-fasting blood sugar values. Verzar (1936) considered that similar effects obtained with adrenalectomized rats were due to the need for cortical hormone in the phosphorylation stage. On the other hand, Deuel *et alii* (1937) have shown that restoration of sodium levels alone in these animals restores carbohydrate absorption and metabolism to normal by removing inanition. Our data are insufficient to enable us to make any differentiation between such influences.

After a further three days' treatment the child was eating and sleeping well, walking about, not sweating, and not irritable, but still objecting to very strong light. No gain in weight had occurred. The injections were then given three times a week, and fourteen days afterwards every symptom had disappeared, and the child had gained twelve ounces in the previous week.

This was an early case, in which photophobia caused the mother to consult an eye specialist. The patient was treated with salt and desoxycorticosterone acetate, with the relief of all symptoms. The lymph glands diminished in size.

CASE XI.—Anne D., aged four years, had suffered from pink disease at the age of eight months, which was severe and lasted for one year. The mother added: "Since then the child has never really recovered. She never has any appetite and sweats periodically. Three months ago the child developed chicken-pox which was closely followed by pneumonia, and her appetite has diminished further. She sweats more and has no energy. If she plays during the morning, she wants to rest all the afternoon. Her hands have lately been pink, cold and clammy. She is very restless at night and inclined to emotional outbursts." Since contracting chicken-pox the child had begun to suffer from asthma.

On examination of the patient, a slight pinkness and distinct coldness of the hands and feet were present, and they were moist. The blood findings were as follows: the plasma sodium content was 300 milligrammes *per centum*, the cell volume was 44%, the hæmoglobin value was 13·9 grammes *per centum*, the plasma protein content was 7·7 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*. The systolic blood pressure was 100 millimetres of mercury and the diastolic pressure was 60 millimetres; the pulse rate was 110 per minute. A twenty-four hour specimen of urine had a volume of 500 millilitres and contained 3·1 grammes of chloride (expressed as sodium chloride).

Treatment with salt was started, and one week later the mother stated that the child had much more energy and was brighter, but the appetite was still poor. "Linguets" of desoxycorticosterone acetate, one milligramme in strength, three per day, were then given to the child, and allowed to dissolve under the tongue. Six days later the mother reported that the child was eating much better, was full of energy and no longer tired easily. The blood findings at this stage were as follows: the plasma sodium content was 330 milligrammes *per centum*, the cell volume was 38%, the hæmoglobin value was 13 grammes *per centum*, the plasma protein content was 7·0 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*.

She continued to do well. The asthmatic attacks disappeared.

This child had a recurrence of pink disease, probably precipitated by a recent virus infection. Response to treatment was prompt. An interesting point is that the asthmatic attacks disappeared. (*Vide infra*, discussion on vegetative adaptation.)

CASE XII.—Paul B., aged six months, had for the last three weeks been miserable and irritable and his sleep had

been poor. His appetite had been lost and his weight was stationary. The child was listless and did not seem to have any power in his muscles. He burrowed into the pillow. Constipation was noticeable and he sweated a lot at night.

On examination of the patient, hypotonicity of the muscles was obvious. A miliarial rash was present over the front and back of the trunk, and there was generalized lymph gland enlargement. Only slight pinkness of the hands was noticeable, but they were cold and moist. The blood findings were as follows: the plasma sodium content was 290 milligrammes *per centum*, the cell volume was 41%, the hæmoglobin value was 13·8 grammes *per centum*, the plasma protein content was 6·7 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*. The systolic blood preasure was 110 millimetres of mercury and the diastolic pressure was 80; the pulse rate was 150 per minute.

Treatment with salt by mouth was begun, one to two teaspoonfuls being given with the food. Four days later the mother reported that the child was eating and sleeping better and was more interested in his surroundings. A week later the child was eating and sleeping well, and was happier, laughing and smiling at times, and using his muscles. His weight was stationary. Injections of steroid, four milligrammes daily, were then begun. The next day it was obvious that the child had developed a severe cold with an inflamed throat and nasal discharge. The mother reported that sleep had been poor the previous night and that he was not eating well, although he was not irritable. Injections were continued daily, and five days later he was once more eating well and was quite happy. It was a further ten days before he was symptom-free on this treatment, and the mother reported a gain of eight ounces in weight. The blood findings at this stage were as follows: the plasma sodium content was 335 milligrammes *per centum*, the cell volume was 39%, the hæmoglobin value was 12·8 grammes *per centum*, the plasma protein content was 6·5 grammes *per centum*, and the non-fasting blood sugar level was 100 milligrammes *per centum*.

This child did not show a quick response to treatment once the secondary virus infection had established itself. This phenomenon has been noted in Addison's disease and is due to increased demand upon vegetative regulation including the suprarenal function.

CASE XIII.—Ian C., aged seven months, had for the last month been miserable and irritable, and his weight had dropped from 17 pounds 6 ounces to 15 pounds 14 ounces. Sleep was poor, and photophobia was present. He had had a rash twice recently, and he sweated a good deal. His hands and feet were cold and moist. He used to pull himself up, but no longer had sufficient energy. He was very constipated.

On examination of the patient, muscle weakness and generalized glandular enlargement were present; there was no pinkness of the hands and feet, but coldness and moistness were apparent. The blood findings were as follows: the plasma sodium content was 280 milligrammes *per centum*, the cell volume was 44%, the hæmoglobin value was 14·6 grammes *per centum*, the plasma protein content was 6·6 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure 100 millimetres; the pulse rate was 180 per minute.

Treatment with salt by mouth was begun, one to two teaspoonfuls daily being given. Five days later the mother reported that the child was sitting up, was eating and drinking more and was much happier, and that he had gained three-quarters of a pound in weight (16 pounds 10 ounces). Sweating and photophobia were still present, and sleep, although improved, was not yet normal. After one week's treatment the hands were warm and the child was happy, smiling, playing and using his muscles. Steroid injections were then given for four days with a complete disappearance of the symptoms. The blood findings were as follows: the plasma sodium content was 360 milligrammes *per centum*, the cell volume was 37%, the hæmoglobin value was 12·4 grammes *per centum*, the plasma protein content was 6·2 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. Injections were then given three times for only one week and the condition of the child remained excellent.

In this case the disease was of one month's duration; improvement was effected by one week's salt treatment, and a complete loss of symptoms occurred after four days' injections with desoxycorticosterone acetate.

CASE XIV.—Jeffrey G., aged eight months, had suffered from chicken-pox one month earlier; he had become miserable and irritable and showed a dislike for the light. He had begun to sweat at night and his sleep had become poor. He had had a sweat rash two days prior to examination, but that had gone. He was eating moderately well. Slight pinkness of the hands and coldness were noticeable. Lymph glands were palpable and the muscles soft.

This child was first examined by a pædiatrician, who, being unable to warn us in time to secure blood specimens, started the salt treatment five days before that was done. The mother reported that as a result of this treatment the child was much more active, with more energy and eating and sleeping better. No sedation had been necessary for two nights. The child was using his muscles and climbing up his cot. The mother stated: "He has made definite improvement the last five days." At this stage the blood findings were as follows: the plasma sodium content was 305 milligrammes *per centum*, the cell volume was 39%, the hæmoglobin value was 12·4 grammes *per centum*, the plasma protein content was 6·3 grammes *per centum*, and the non-fasting blood sugar level was 70 milligrammes *per centum*. The systolic blood pressure was 130 millimetres of mercury and the diastolic pressure 100 millimetres; the pulse rate was 160 per minute.

After one week of treatment with salt alone, the child was playing and smiling sometimes. There was some degree of irritability, but much less. He had gained three ounces in weight and was eating well, and the hands were warm. Daily injections of four milligrammes of steroid were given.

The child contracted a severe cold, and some degree of irritability and anorexia was present for the next ten days, although he slept well and the muscles remained firm and active. Recovery from the cold was followed by uninterrupted general improvement. The blood findings at this stage were as follows: the plasma sodium content was 330 milligrammes *per centum*, the cell volume was 38%, the hæmoglobin value was 12·4 grammes *per centum*, the plasma protein content was 7·2 grammes *per centum*, and the non-fasting blood sugar level was 110 milligrammes *per centum*.

In this case, as in the case of Paul B., the presence of a virus infection rendered the treatment less effective. Doubtless increased dosage of steroid would counteract this adverse influence.

CASE XV.—Raymond K. was aged one year and eight months. For this report we are indebted to Dr. S. Downing, of Mount Barker, South Australia. Raymond K. had a history of irritability, miserableness and failure to take food, extending over a period of four months. He sweated a great deal at night and had lost five pounds in weight. His sleep was poor. He had stopped walking and wanted to rest all day. His hands and feet were cold, red and swollen. For the past six weeks he had had liver injections twice a week with no improvement or gain in weight. Heavy sedation was necessary.

For the first week of treatment salt was given by mouth, one to two teaspoonfuls per day with the food, and desoxycorticosterone acetate (two milligrammes three times a week) was given by injection. In the second week the dose was raised to four milligrammes every third day. After the second injection the appetite improved, and after the third, sleep became much better and the hands less red. Then a surprising thing happened—there was rapid improvement. The child developed an interest in his surroundings, started to run about and to sleep and eat normally, and gained nine ounces in nine days. Four weeks from starting the injections he had gained two pounds in weight and showed little or no signs of the disease.

The parents then moved to Victoria. By a personal letter to the doctor in charge of the child in that State, it was asked that the treatment should be continued; a fortnight after having last examined the child, he reported a further gain of nineteen ounces.

This child was originally referred to in the preliminary report as having a definite craving for salt. He had been previously given the usually accepted treatment for this disease, with no improvement. After salt and steroid treatment he made a dramatic recovery.

CASE XVI.—Richard P., aged six months, was admitted to the Adelaide Children's Hospital on September 23, 1949, with a history of irritability and severe photophobia of two months' duration. Sweating was excessive and a generalized miliarial rash was present. Pink, cold, swollen extremities were noticeable. Feeding was difficult but adequate. Lately the child had lost some hair, and the weight, previously 15 pounds four ounces, was now 14 pounds. The inguinal glands were palpable and pronounced muscle paresis was present. There had been one or two loose bowel actions

before his admission to hospital. The plasma sodium content was 285 milligrammes *per centum*.

On September 28 the bowel actions became more frequent, and on October 1 the child had eight fluid bowel actions and appeared dehydrated. Normal saline was given intravenously for thirty hours; photophobia, irritability and pinkness of the hands promptly disappeared. The plasma sodium content was 340 milligrammes *per centum*.

The clinician in charge of the patient then substituted one-fifth normal saline with 4% glucose solution for the normal saline. (This procedure illustrates the existing confusion on the subject, for although the glucose aimed at the correction of low osmotic pressure in the vascular system, the electrolytic balance remained adverse and detrimental in effect. Moreover, as the glucose became condition. He became comatose and was taking very little fluid by mouth—about seven ounces per day. The sister of the ward, the nursing staff and the superintendent were of the opinion that the child would soon die. The house surgeon wrote in the case notes: "The child looks ghastly."

On October 14 we were allowed to do what we could for the child. Serum (100 millilitres) was given daily with normal saline and 5% glucose solution for four days. After three days the child showed considerable improvement; he began to take food by mouth—six ounces every four hours. The child was hungry and took notice of his surroundings; but above all the motions became paste for the first time. After four days of this treatment, during which period 400 millilitres of serum had been given together with the salt and glucose (all intravenously), the blood findings were

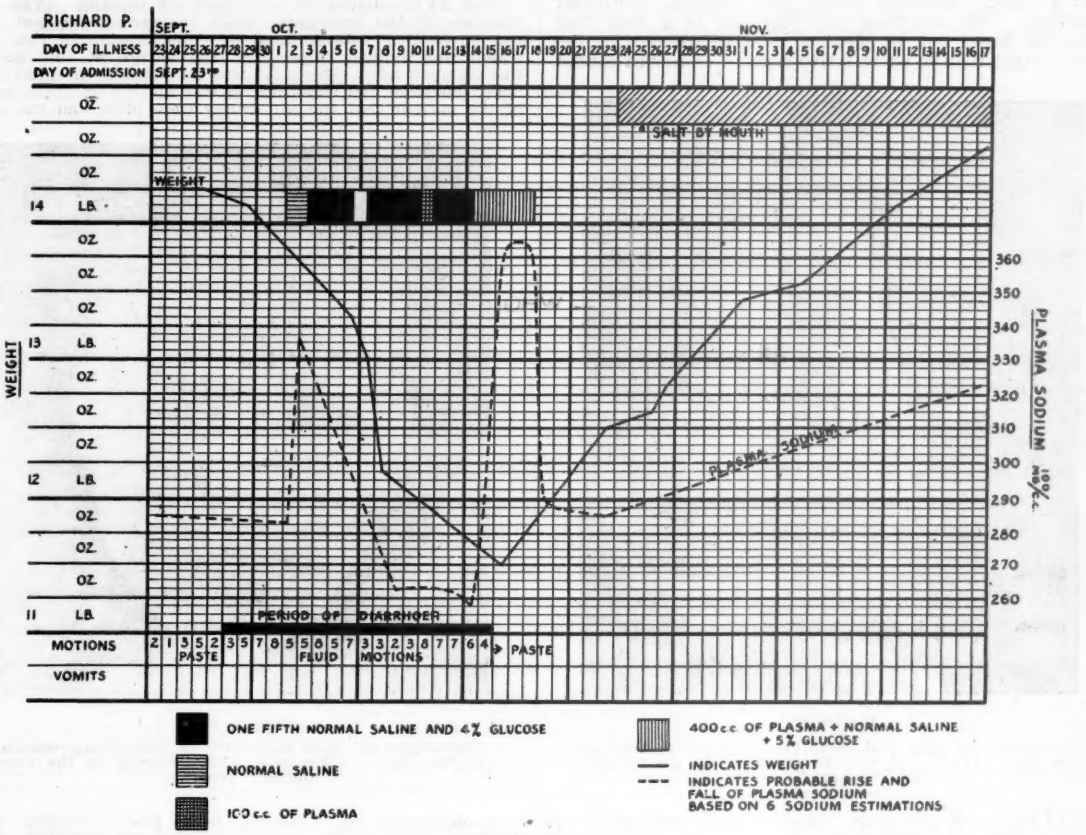

FIGURE IV.

metabolized, even the osmotic effect was temporary.) Photophobia, irritability and pink hands promptly returned, the diarrhœa continued, and loss of weight was accelerated. (See Figure IV.)

The administration of hypotonic saline was continued, and on October 9 the plasma sodium content was 260 milligrammes *per centum*. Weight loss continued and with it the diarrhœa. No pathogenic organisms could be isolated from the fæces. The diarrhœa did not respond to chemotherapy. The child's condition rapidly deteriorated, and on October 10, 100 millilitres of serum were given with slight clinical improvement. The hypotonic saline infusion was continued. The blood findings at this stage were as follows: the plasma sodium content was 260 milligrammes *per centum*, the cell volume was 51%, the hæmoglobin value was 16·1 grammes *per centum*, the plasma protein content was 5·6 grammes *per centum*, and the non-fasting blood sugar level was 110 milligrammes *per centum*.

It should be realized that in correcting hæmoconcentration the plasma protein level should lie somewhere in the region of 3·9 grammes *per centum*.

On October 12 administration of hypotonic saline was continued, with a further rapid deterioration in the child's as follows: the plasma sodium content was 360 milligrammes *per centum*, the cell volume was 44%, the hæmoglobin value was 14·6 grammes *per centum*, the plasma protein content was 5·4 grammes *per centum*, and the non-fasting blood sugar level was 50 milligrammes *per centum*.

On October 17 it was admitted by all that clinical improvement had occurred. The child was taking food well by mouth. The intravenous therapy was stopped; twenty-four hours later the child had a convulsive seizure and was comatose and cyanosed for a short time, but recovered later in the day. Improvement continued, the child took food well, and the motions were paste.

On October 23 the irritability and photophobia, which had seemed to be less obvious during the extreme prostration of this child, now seemed to come more into prominence. The hands were pink but not cold. On October 25 the administration of salt by mouth was started, one teaspoonful being given with the food. Progress continued. On November 1 the child was feeding well, bright-eyed and interested in his surroundings, and the weight was now climbing steadily. Irritability was lost. On November 3 the blood findings were as follows: the plasma sodium content was 300 milligrammes *per centum*, the cell volume

was 42%, the hæmoglobin value was 13·3 grammes *per centum*, the plasma protein content was 7·4 grammes *per centum*, and the non-fasting blood sugar level was 90 milligrammes *per centum*. Photophobia and pinkness of the hands were now lost, and the child laughed and smiled.

On November 9 the child was sitting up and actively using his muscles, well and happy, but under weight. On November 16 the blood findings were as follows: the plasma sodium content was 320 milligrammes *per centum*, the cell volume was 38%, the hæmoglobin value was 12 grammes *per centum*, the plasma protein content was 6·4 grammes *per centum*, and the non-fasting blood sugar level was 80 milligrammes *per centum*. The weight had all this time been steadily climbing. On November 19 the child was discharged from hospital.

This child, suffering from pink disease, developed diarrhœa. (We attribute this diarrhœa to a fluid leak from the bowel due to the low osmotic pressure of the blood, rather than to an infective cause.) Diarrhœa caused

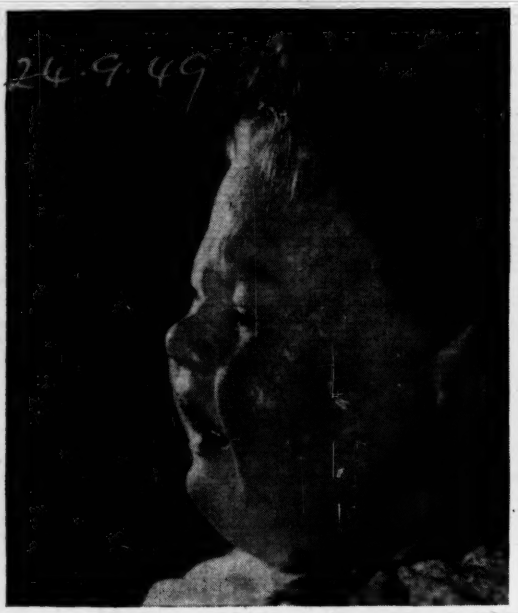

FIGURE V.

Photograph of child B.R. showing non-pitting œdema of the face. (This case was discussed in the preliminary report.)

loss of salt from the bowel. Normal saline was given for thirty hours. The electrolyte was temporarily restored to the blood, and photophobia, irritability and redness of the hands disappeared as a result. Then the hypotonic saline and glucose solution was substituted for the normal saline. There was a resultant further dilution of the electrolyte in the blood. Photophobia, irritability and pink hands returned. Diarrhœa and salt loss by the bowel continued and the child's condition rapidly deteriorated; little food was taken by mouth, and thus the exacerbating factor of hypoproteinæmia developed.

The child now was unable to hold water in the bloodstream. Hæmoconcentration increased rapidly. The child was on the verge of shock, collapse and death. Plasma and normal saline and 5% glucose solution were then given for four days. The plasma protein level did not rise immediately, because protein first replaced labile tissue protein. The plasma sodium level temporarily rose, hæmoconcentration lessened, the child showed improvement and started to take food, and the diarrhœa stopped. The intravenous therapy was stopped and the plasma protein level, which was still low, was unable to maintain the water content of the blood and there occurred a rapid loss of water and sodium through the kidneys. The sudden movement of extracellular fluid into the tissue cells producing turgor of cerebral cells was doubtless the cause of the convulsive seizure.

Progress then continued. Salt was given by mouth and the salt loss was gradually made up. The child ate well and was given expressed breast milk, and gradually the protein level in the plasma rose. Hæmoconcentration decreased still further and gradually the plasma sodium level rose. Irritability, photophobia and pinkness of the extremities disappeared and with a rapid gain in weight recovery was complete.

This is a classical picture of salt-water imbalance exacerbated by hypoproteinæmia and diarrhœa.

CASE XVII.—James W. was aged six months. (The significance of the statements made concerning the last case can be further substantiated by consideration of this one, which was studied before the true nature of this disease was appreciated.) The child was admitted to hospital with acute diarrhœa and vomiting. It was noticed on examination of the patient that the ear drums were pink, and the child

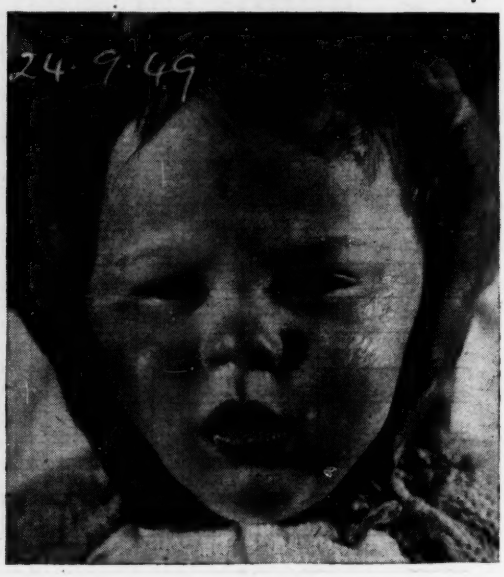

FIGURE VI.

Photograph of child B.R. showing non-pitting œdema of the face. (This case was discussed in the preliminary report.)

was diagnosed as suffering from gastro-enteritis with bilateral *otitis media*. Sulphadiazine and penicillin were given, but the fluid motions continued. No pathogenic organisms were isolated from the fæces. A few days after his admission to hospital it was noticed that the child displayed a dislike for the light, that his hands were cold and pink, that his nose was pink, and that he was irritable. The question of pink disease was considered by the clinicians and dismissed and not even mentioned in the case notes.

On investigation of the patient it was found that the blood pressure was 130 millimetres of mercury, systolic, and 80 millimetres, diastolic, and that the plasma sodium content was 305 milligrammes *per centum* and the hæmoglobin value 14 grammes *per centum*. The erythrocytes numbered 5,600,000 per cubic millimetre and the leucocytes 14,000 per cubic millimetre.

A week after the child's admission to hospital the house surgeon's notes read as follows: "Still having some fluid motions. Both drums remain pink, temperature normal, not taking food at all well, some vomiting, no cause found for the diarrhœa." The same night he wrote: "Tissue turgor much worse. Both ears pink, but not, in my opinion, deserving of opening at present. Diarrhœa and vomiting persists."

One hundred millilitres of normal saline were given intravenously followed by one-fifth normal saline and glucose

solution. The diarrhœa subsided a little. Paracentesis disclosed no abnormality. Three days later the intravenous drip administration was replaced by gastric drip administration, hypotonic saline and glucose solution still being given. The diarrhœa continued.

The left ear drum was again opened without result. Vomiting then became severe in spite of the gastric drip therapy, and dehydration was severe. Two hundred millilitres of normal saline were given intravenously, and then one-fifth normal saline and 4% glucose solution were again substituted. The ear, nose and throat surgeon was consulted and his comment was as follows: "I don't seem very convinced about toxicity from latent mastoiditis, but the only proof is exploration, which I would undertake at an opportune time."

Diarrhœa still continued, and after a further four days streptomycin was given orally and the penicillin and sulphadiazine treatment was stopped. One-fifth normal saline and glucose solution was still being given. At this stage the plasma sodium content was 280 milligrammes *per centum*, the hæmoglobin value was 18·8 grammes *per centum* and the plasma protein content was 4·9 grammes *per centum*.

Four days later the mastoids were opened and the right side was reported to be normal and the left to contain some degree of necrotic material. "The child looked fairly ghastly." One hundred millilitres of serum were given and "Coramine" was also frequently administered. The condition of the child rapidly deteriorated. Five days later the plasma sodium content was 260 milligrammes *per centum* and the plasma protein 3·5 grammes *per centum*. The house surgeon wrote in the case notes: "Not vomiting; still has diarrhœa."

The child's condition then started to deteriorate more rapidly. Two days later there was a "sudden vascular collapse" with cyanosed extremities. The fifth-normal saline was then changed to normal saline, 200 millilitres being given. The child remained comatose and died two days later.

This child was admitted to hospital with diarrhœa and vomiting. No cause for these was established. Repeated bacterial examination of the fæces gave negative results. Some signs of pink disease were displayed. A low plasma sodium level was detected, which we now realize characterizes the condition of pink disease. Unfortunately confusion was repeatedly caused by the presence of pink ear drums, it being thought that bilateral *otitis media* was present and that this was a parenteral infective basis for the diarrhœa; but in pink disease pink ear drums are to be expected. This was emphasized by Derham (1935) at a meeting of the British Medical Association.

Diarrhœa relentlessly continued. Three weeks of intravenous hypotonic saline therapy were interspersed with the administration of two small amounts of normal saline and serum. The plasma sodium level progressively fell and hæmoconcentration was indicated by the single hæmoglobin estimation of 18·8 grammes *per centum*. Hypoproteinæmia obviously became progressively worse. Death occurred from vascular shock, induced by dehydration and excessive salt loss.

It is specially to be noted that the substitution of the intravenous for the gastric administration of hypotonic saline in no way changes the effect. Before absorption salt is withdrawn from the blood to bring the hypotonic saline to isotonicity. The net result is therefore the same—that is, production of water diuresis and increased salt loss. In the final stage, acidosis owing to depletion of available sodium ions might well have been expected.

In this connexion it is of interest to record the fact that two patients with pink disease treated with gastric lavage for the removal of mucus died within a few hours, in our opinion from acute hæmoconcentration due to the passage of salt from the blood into the stomach.

Conclusions from a Study of the Cases.

Salt.

Ordinary salt in quantities of one to two teaspoonfuls per day, placed either in the food or in the milk, is of great benefit to these children at any stage of the disease. In milder cases salt alone may effect a cure. It may relieve the irritability and sleeplessness, anorexia, fatigue and immobility before even a demonstrable elevation of the blood sodium level has occurred. This would indicate of what great importance the sodium ion alone is in maintaining important physiological processes in the body. When lassitude is present, and more noticeably in older children, the salt may have quite a dramatic effect.

Salted food is taken readily, the patients having a liking, and indeed sometimes a craving, for it.

Salt and Desoxycorticosterone Acetate.

By cutting down the salt excretion by the administration of the synthetic steroid, the symptoms of pink disease can be removed in a short space of time. If salt is given by mouth and if four milligrammes of steroid are given daily by intramuscular injection, photophobia, irritability, sleeplessness, anorexia, constipation, sweating and pinkness and coldness of the extremities will be rapidly reduced, if not completely eradicated, within one week. No sedation is necessary.

If the treatment is stopped the symptoms will rapidly reappear, only to disappear again on the recommencement of treatment.

Once the symptoms of this disease have been reduced by a week's treatment as suggested, it is necessary to determine the amount of steroid required to maintain the child. This dosage may be four milligrammes given by injection every other day, or perhaps two milligrammes twice a week. Every case will vary. It may be necessary to continue daily injections for several days or weeks, or salt alone may be all that is needed.

Weight.

The weight does not necessarily increase in proportion to the general improvement. Of several possible causes there is the significant one that the restoration of tissue protein is slow, and only when considerably restored does tissue protein appear to "hold" the equivalent amount of water. In the great majority of cases, however, soon after the commencement of treatment the weight chart will show improvement.

Hæmoconcentration.

Hæmoconcentration is present in all cases, and it can be seen that it is reduced by treatment and reappears again on the cessation of treatment; but as the plasma sodium level falls, so the hæmoconcentration rises and *vice versa*.

These two findings, therefore, are of diagnostic import and of some value in gauging the severity of a case.

Diagnosis in Older Children.

In older children, irritability, failure to gain weight, sleeplessness and lack of energy are the abnormalities to be noted. If one thinks only in terms of pinkness of the hands and photophobia, the diagnosis may be missed.

It must be the experience of every general practitioner and pædiatrician that he has had patients displaying these symptoms and that the cause has eluded him. The estimation of plasma sodium content and hæmatocrit cell volume will be of great help in differential diagnosis in such instances. The case of Gillian C. illustrates these points adequately.

It can be seen also from a study of the case of Anne D. that although this child had suffered from this condition when she was a baby, she had never made a complete recovery, owing, in our opinion, to delayed response of the suprarenal gland to growth and development. As a result of the severe infection, her suprarenal glands had been placed at a further disadvantage, so that a mild recurrence of pink disease became clinically obvious.

Diarrhœa and Secondary Infections (Severe).

When diarrhœa and secondary infections appear, it is necessary to have a knowledge of the plasma protein level in the blood and of the degree of hæmoconcentration. Plasma protein must be given intravenously, together with normal salt solution and glucose, and if necessary desoxycorticosterone acetate must be given intramuscularly. The fluid balance chart of the child, however, must be watched carefully. In other words, reduce the hæmoconcentration with saline and restore the depleted plasma

protein independently of any chemotherapy that may be advisable. Hypotonic saline should never be administered under any circumstances.

DISCUSSION.

Pink disease, together with all those manifestations of the condition that characterize it, but which, in the absence of red, cold extremities are too often overlooked, is a condition found during the first eight years of life, and chiefly in the first four. This coincides with the period of maximum post-fœtal development of the suprarenal glands. During fœtal life there is hyperplasia of the *zona reticularis* and *zona fasciculata*, and the cortex at birth is therefore greatly swollen and in contrast with an ill-developed medulla, the only pheochrome cells of which are found grouped round the greater veins.

Birth is associated with an immediate and dramatic change (Elliott and Armour, 1911; Kern, 1911; Thomas, 1911), in which there occurs hyperæmic involution of the innermost layer of the cortex, extending, during the second month, outwards into the cortical cells, in which degenerative changes take place throughout the first years of life. These cells are replaced by connective tissue, which gives the appearance of a thick capsule surrounding the medulla. From the second year onwards until adolescence this "capsule" in turn disappears as it is invaded by the now rapidly developing pheochrome tissue, until the latter comes into contact with the cortical tissue.

For our purposes it is most important to note that this latter stage is reached at about eight years and coincides with complete morphological development of the cortex. Thereafter only the medulla increases in size, ceasing its growth at adolescence (Lewis and Pappenheimer, 1916).

There are therefore two phases of suprarenal development, one intrauterine, the other post-natal. The former is related to the influence of the constant internal environment of the *liquor amnii*, the maternal blood transport of gases, metabolites and nutrients, and the claims of rapidly multiplying cells whose cytoplasm contains twice as much water as that of the adult, and with proportionately one-quarter the amount of water in the extracellular phase.

At birth the environment changes almost on the instant to one involving varying external temperature, higher oxygen and lower carbon dioxide tension, and a newly functioning digestive system shortly to develop a bacterial flora of its own.

Goldzeiher (1934) has reported delayed or absent cortical involution in cases of congenital cardiac defect with cyanosis, showing that gaseous exchanges play an important role as an environmental influence, whilst the hypoplasia of the cortex in the anencephalic fœtus emphasizes the significance of the fœtal cortical tissue in processes of rapid cellular differentiation and growth.

The second or post-fœtal stage begins with a destruction of cortical tissue which had fœtal functions, and continues through the early years of life, during which a new suprarenal gland develops to meet different environmental needs. The medulla plays an increasingly important part, being involved together with the cortex in heat production and regulation (Cramer, 1928). The beginning of this post-fœtal life is associated with rapid destruction of red corpuscles and their subsequent replacement in diminished number from new sources, the new corpuscles containing hæmoglobin with dissociation characteristics suited to the altered levels of gaseous exchange. There is simultaneously a rapid loss of body water amounting to 10% of body weight, with parallel decrease in sodium and chlorides (Stearns, 1939).

That this period of early infancy is one dominated by the altering function of the suprarenal tissue finds illustration in the interesting and otherwise unexplained fact of a large sodium reserve in fœtus and infant—a reserve greatly in excess of the total calculated on the basis of extracellular water. This reserve, largely in bones, is drawn upon to replace loss and vitiates much published work on sodium and total base in early infancy (Bruch and McCune, 1936). This reserve of salt, in our opinion, plays an important role in determining whether the pink disease syndrome will develop, and in the insidious nature of the onset of the syndrome when it does.

Jaudon (1946, 1948) reviews the literature relating to the diseases of the early weeks of infancy and contributes much valuable information, which goes far to establish suprarenal cortical hypofunction as an underlying cause of a wide variety of clinical manifestations. He describes the syndrome as nausea, regurgitation, vomiting, dehydration and collapse, and shows that it is related to excessive renal loss of sodium, chloride and water, due to temporary low function of the suprarenal cortex. In his earlier nine cases were present general debility, an appearance of impending shock, and a state of dehydration which was refractory to the administration of isotonic saline and glucose solution, though favourably reacting to cortical extract. He could find no intestinal infection to account for the diarrhœa present in these cases.

Our own cases of pink disease demonstrate similar features, and in our opinion are due to a similar though less acute cause than that of early post-natal accelerated cortical involution. To borrow from Selye (1946), we are dealing with the adaptation syndrome of infants during their vegetative adjustment to post-fœtal life. A simplified illustration may clarify what is otherwise complex and difficult to grasp. Hicks and Hone (1935) reported a case of extreme Simmonds's cachexia, in which restoration to normal was achieved by some months' treatment with prolan, followed for a later period with preloban. At the present time this patient weighs over ten stone and is vigorous and well and six months pregnant. Considered from the angle of organ pathology, an anterior lobe of the pituitary gland, damaged in this case by the virus of mumps, could not be restored to normal function. Considered from our standpoint, the case can be illustrated by reference to two children on a see-saw, one too heavy, holding its end down, the other in the air unable to restore balance by moving further out. If a third person stands in the centre and adds weight to the appropriate side until the children adjust the weight-distance ratio, balance can be restored. The balance of adaptation being upset for some reason, it can be restored by the administration of salt *per os* if imbalance is slight or noted early, of salt with desoxycorticosterone acetate if the imbalance is severe or noted later, and of salt intravenously as isotonic saline *plus* desoxycorticosterone acetate if the condition is still more severe or noted even later. This later stage may require the intravenous administration of plasma protein to restore plasma protein and colloid osmotic relations, and labile cellular protein (Whipple, 1947). This is the stage of so-called "gastro-enteritis", which has given rise to the fear of "cross-infection". It is probably due to the failure of intestinal absorption of glucose *plus* low plasma colloid osmotic and electro-osmotic pressures, leading to increasing capillary passage of fluid into the bowel.

A patient with Addison's disease treated with whole suprarenal gland (Hicks and Mitchell, 1935) readily developed diarrhœa if he over-exerted himself, and another, who otherwise lived a reasonably normal life, developed an Addison's crisis with diarrhœa during a febrile attack of influenza; a study of the literature provides an overwhelming mass of evidence from which but a few significant examples only can be cited here. Selye alone publishes a bibliography of 698 references on the topic of the adaptation syndrome.

Relevant to our view of suprarenal hypofunction are the observations of Hislop (1938), who reported on the favourable results of treatment in 19 cases of infantile nutritional disorders by means of desoxycorticosterone acetate. Szaz (1939) reports in like manner on 20 patients treated with cortical extract, salt and glucose. He also records cyanosis in the acute stage of his cases, and this is highly suggestive of hæmoconcentration. Aquirre, Tahier and Delpino (1941), to whose paper we have only an abstract reference, report on three patients with cœliac disease responding favourably to cortical extract. This again emphasizes the related failure in carbohydrate and fat absorption and metabolism in cortical hypofunction. In the case of Simmonds's disease and in a similar but

milder case of pituitary dysfunction as well as in Addison's disease, Hicks has reported a revulsion from fat and carbohydrate in the food, which was changed into a craving for sweets by oral administration of whole suprarenal cortex.

Pink disease or infantile acrodynia has received its many names from two main characteristics—namely, the colour, swelling and desquamation of the extremities, and the muscular atonia. There is, however, a large list of symptoms and signs, which do not readily fit any simple designation. This is responsible for failure hitherto to find a cause, although some signs if followed would have disclosed it: we refer to the persistent leucocytosis and polycythæmia. The following is a list of phenomena displayed in the course of the disease: loss of vivacity, lack of interest, listlessness, irritability, bad temper, muscular weakness, inability to stand, disturbances of sensation (pain, heat, tingling, prurigo), loss of tendon reflexes, photophobia, loss of appetite, insomnia of an intractable kind, excessive sweating, especially of extremities, desquamation and even loss of nails, septic eruptions and even gangrene, stomatitis and loss of teeth. Tachycardia is constant.

This is indeed a formidable list, but it yields to analysis in terms of suprarenal hypofunction.

The loss of water and salt leads to hæmoconcentration and to an increase in the water content of cells. The ionic imbalance between the extracellular and intracellular phases is doubtless involved in a manner still unknown to us, whilst altered carbohydrate metabolism among other results of diminished production of corticosteroids and/or of adrenaline and nor-adrenaline has its influence upon muscular metabolism and tone.

Thus we have hæmoconcentration and cellular turgor combined with anhydræmia and thirst, and muscular weakness with loss of reflex response.

The "trophic" changes become nothing more than the secondary result of cellular turgor, and the disordered sensations such as burning and tingling in cold extremities become a manifestation of stagnant anoxia.

Irritability and photophobia can be similarly explained in terms of cellular turgor and/or ionic imbalance across the cellular interface, and the apathy and listlessness reflexly in terms of loss of general muscle tone.

Susceptibility to infection with weakened resistance finds an explanation in the disabled cellular metabolism, which grows worse as continued lack of appetite leads to hypoproteinæmia.

The diastolic and systolic blood pressures are raised, especially the former, owing to reduced "run-off" caused by the raised viscosity, and the pulse rate rises owing to response of carotid sinus chemoreceptors. In infants heat regulation is not well adjusted for reasons connected with the very problem lying at the kernel of this disease—namely, the undeveloped sympatho-adrenal system. Sweating therefore could be evidence of an attempt to cool the body when, owing to hæmoconcentration, cutaneous vasodilatation is less effective. The raised body temperature indicates a failure in heat loss.

The constipation which characterizes the condition could be explained in terms of muscular hypotonia and anhydræmia; but the diarrhœa with or without vomiting seen in the later stages and commonly interpreted as gastro-enteritis seems to us to be associated with hypoproteinæmia and consequent excessive passage of water and electrolytes across the capillary barrier. At the same time the condition may arise from, or be contributed to by, deterioration in the absorption of glucose and fat. Pain in the abdomen without evidence of cause has been noticed by many observers. One is reminded of its occurrence in violent form in some crises of Addison's disease.

The glandular enlargement seen in these cases may well be a manifestation of the "alarm reaction" of Selye, which may also explain coincidental allergic phenomena (*vide* the case of Anne D., herein reported).

Without carrying the analysis further, we have done enough to show that a rational explanation of the multiplicity of the manifestations of pink disease lies in a disturbance of suprarenal adaptation to post-fœtal life. This adaptation is on anatomical grounds, not completely possible before the eighth year, and it is perhaps not too fanciful to suggest that ecology plays a part in the establishment of a working relationship between the infant, its foodstuffs and its intestinal and upper respiratory flora.

This explanation of the syndrome of pink disease gains support from the excellent results of therapeutic measures taken to restore plasma sodium and chloride levels and to raise the renal threshold for salt and the corticosteroid level of the system generally. Treatment along these lines, therefore, aims to restore the temporarily lost balance of the adaptation of the vegetative system. At first it can be restored by salt alone (mention has been made of the large fœtal salt reserve), and at later stages desoxycorticosterone acetate is required in addition. Intravenous medication is required only in severe late stages, which should now be seldom seen.

On the other hand, a disturbance of the adaptation syndrome may be precipitated by any condition, whether non-specific, such as burns, or by an infection. The hydrolability of the infant which characterizes it must be borne in mind and recourse to salt and desoxycorticosterone acetate may well prove a valuable emergency therapy in a wide range of disturbances in infancy and childhood. In any case, an estimation of packed cell volume will always provide evidence of anhydræmia, and a low plasma sodium level will confirm the existence of a possible adaptation syndrome.

If it is correct to interpret these conditions as "diseases" of adaptation, it will remain for future workers in possession of more accurate statistical evidence to show whether they are manifestations of civilized life and are on the increase.

Pink disease or infantile acrodynia is a syndrome of disturbed adaptation of the vegetative adjustment to post-fœtal life. It is characterized by hypofunction of both the cortex and the medulla of the suprarenal gland, leading to a low renal threshold for sodium and chloride, with consequent loss of these as well as of water. As a result there occur anhydræmia, hæmoconcentration and a shift of water into the tissue cells owing to raised electrolytic osmotic pressure in the intracellular phase. The evidence indicates that supervening "gastro-enteritis" is a manifestation of the salt-water imbalance and disturbed carbohydrate metabolism aggravated by low colloid osmotic pressure of the plasma due to hypoproteinæmia.

The diagnosis is confirmed by the presence of hæmoconcentration and low plasma sodium levels.

The manifold symptoms and signs of the condition are explicable in terms of anhydræmia, hæmoconcentration, cellular turgor, raised blood viscosity, lessened control of heat loss, stagnant anoxia, loss of salt and impaired carbohydrate metabolism.

Prevention can be ensured by oral administration of salt on recognition of the early signs of irritability, listlessness and muscle weakness. Cure can be effected by similar treatment in the early stages, but in the later or more developed types of the disease injections of desoxycorticosterone acetate are indicated. In severe cases or in cases exacerbated by intercurrent illness the intravenous administration of isotonic saline with larger doses of desoxycorticosterone acetate is necessary. If vomiting and diarrhœa threaten rapid collapse, the intravenous administration of plasma protein is essential and life-saving.

The importance of recognizing suprarenal hypofunction as a causal or aggravating influence in the diseases of early infancy and in childhood has been emphasized by other workers, and their conclusions are confirmed by the present work on 37 cases of pink disease.

SUMMARY.

1. The following conclusions are based upon clinical and laboratory studies of 37 cases of pink disease or infantile acrodynia. Sixteen of the patients collected after the nature of the condition had been recognized have all been successfully and rapidly restored to normal health.

2. The condition is fundamentally an adaptation syndrome, the manifold manifestations of which are causally related to hypofunction of the suprarenal gland, which is

responsible for a lowered renal threshold for sodium chloride.

3. Excessive loss of sodium chloride from the extracellular fluid leads to relatively increased electrolyte concentration in the tissue cells, with consequent movement of water from the extracellular phase, leading to cellular turgor and hæmoconcentration.

4. The hitherto inexplicable complexity of symptoms and signs finds complete elucidation in terms of hæmoconcentration, raised blood viscosity, diminished blood volume and tissue anoxia, together with ionic imbalance between extracellular and intracellular phases.

5. Diarrhœa and vomiting, by rapidly accelerating water and salt loss, can precipitate vascular shock due to excessive hæmoconcentration and failure of venous return. Gastric lavage and also the intravenous administration of hypotonic saline even with added glucose are therefore dangerous.

6. Poor appetite in these cases leads to hypoproteinæmia, the effects of which, in terms of lowered colloid osmotic pressure of the blood, are greatly to increase water loss, dehydration and tendency to shock. It is reasonable to suppose that the fear of infective gastro-enteritis in these cases has arisen from the tendency to diarrhœa and vomiting. However, this is caused, in our opinion, by the passage of fluid from the capillaries to the alimentary canal owing to the hypoproteinæmia, possibly exacerbated by impaired absorption of glucose.

7. The cause and treatment of the syndrome are discussed in terms of post-natal development of the medulla and cortex of the suprarenal gland. Oral administration of sodium chloride, with or without desoxycorticosterone acetate (depending upon the duration or severity of the illness), will restore the salt-water balance, with complete and rapid abatement of symptoms. The oral administration of salt alone in the prodromal stage should prevent the condition from developing and is indicated as an expedient in marasmic and related conditions of children.[1]

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[1] For example, the syndrome of the "nervous child" and "cyclical vomiting".

POLYARTHRITIS PRECIPITATED BY MYOCARDIAL ISCHÆMIA.

By MICHAEL KELLY,
Melbourne.

SINCE the first description by T. Howard (1930) of five cases of periarthritis of the left shoulder complicating coronary disease, many examples have been reported. Earlier, Gibson (1905) had described wasting of shoulder muscles and sensory loss in the arm, while Schmidt (1922), Libman (1927), and Eckerson, Roberts and Howard (1928) had observed pain in the shoulder, without limitation of movement, as a sequel to *angina pectoris.*[1] Edeiken and Wolferth (1936) reported 14 cases, in which various degrees of disability of the shoulder followed myocardial infarction; while Ernstene and Kinell (1940) reported 17 cases and Askey (1941) 22. Other writers on the subject were Boas and Levy (1937) and Spillane and White (1940).

Case I.

The patient, W.R., is a man, aged sixty-six years. In February, 1948, he first attended the out-patient clinic of the Royal Melbourne Hospital with anginal pain and shortness of breath on effort. In May, 1948, continuous pain was felt in the left shoulder and then in the right. Abduction of his arms became painful, so that he could not remove his coat. In September and October the wrists became painful and swollen and the fingers were stiff and swollen.

[1] Steinbrocker *et alii* (1948) give Osler ("Lectures on Angina Pectoris", 1897) the credit for being first in this field; he mentioned a "motor disability of the shoulder" that sometimes followed *angina pectoris.*

When he was first examined in the arthritis clinic on November 24, 1948, he was almost helpless, with limitation of abduction of both humeri, the left being more severely affected than the right. Both wrists were swollen and immobile, and tender, especially on the palmar aspects. The fingers were œdematous and the hands could not be closed.

The wrists were immobilized in plaster of Paris for two weeks. The swelling and tenderness subsided, and the fingers became mobile again. The shoulders were treated by the injection of procaine into tender spots in the trapezius muscle. The right shoulder was restored to full painless range within six weeks, and the left within ten weeks. In February, 1949, the wrists and fingers swelled again for a few days, but at his last visit on March 2, 1949, there was little disability.

In June and July, 1949, he spent two weeks in Dr. K. Fairley's ward with congestive heart failure and was discharged to rest in bed at home. On July 20 he wrote, stating that the arthritis of his wrists and shoulders had not returned.

Case II.

In Case II extreme wasting of the muscles combined with fixation in adduction to give a classical picture of "frozen shoulder", with radiation of myalgic pain to the occiput.

G.S., a diabetic, aged sixty years, suffered for a few years from angina of effort, with occasional rheumatic pains in his right shoulder that did not seem to be related to the cardiac pain. He collapsed with a coronary occlusion and spent two months in bed. Three months later he had continuous pains in the left side of the neck and the shoulder, sometimes shooting up to the occiput. Examination revealed extreme wasting of the deltoid muscle, with gross limitation of abduction and external rotation of the humerus. His pulse was rapid and regular, and he was short of breath.

Injection of procaine into tender spots in the trapezius abolished the stiffness in the neck and the pain that radiated to the occiput, but the shoulder remained stiff and painful. He died six months later.

Changes in the Hand.

In the three cases reported by Meyer and Binswanger (1942), swelling of the left wrist and finger joints followed myocardial infarction. In every case the swelling subsided within a few months, but the patients all died suddenly within eighteen months. Kehl (1943) described six cases of Dupuytren's contracture and other chronic changes in either hand, while Johnson (1943) recorded that in 39 out of 178 cases of infarction, painful swollen fingers developed. In some cases the soft tissues became atrophic and a condition resembling sclerodactyly developed. Shapiro, Lipkis and Kahn (1947) observed ulceration of the hands after myocardial infarction.

Multiple Joint Involvement.

The changes, either in shoulder or in hand, are not limited to the left side, and spread to involve other joints is not unknown. In 29 of Johnson's cases, periarthritis of one or both shoulders developed in addition to the dystrophy of the hands. In several of Ernstene and Kinell's cases the disability of the shoulder was followed by rheumatoid changes in other joints. In Case I in the present paper both shoulders and both wrists were involved, with swelling and stiffness of the fingers.

The periarthritis of the shoulder that follows myocardial ischæmia exactly resembles that due to rheumatism or to injury. There is every gradation between mild "arthralgia" and profound articular disorder with severe wasting and limitation of movement. Degenerative changes may occur in the capsule of the joint; in one of Edeiken and Wolferth's cases X-ray examination showed calcification in the supraspinatus tendon.

To Duplay (1872), who suggested the term, periarthritis meant only subacromial bursitis. The subacromial bursa, which plays such a large part as a supplementary joint in shoulder movement, he named the "periarthros". He thought that it was chiefly involved in painful stiffness of the shoulder, and that the shoulder joint itself escaped. Of this, however, we have no proof, and if the shoulder was accessible to inspection and palpation like the knee or the ankle, I have no doubt that "arthritis of the shoulder" would be diagnosed more frequently.

In arthritis that follows myocardial ischæmia we are provided with a human experiment in which the process begins in a certain joint in response to a known stimulus. Useful lessons may be learned from these examples of rheumatic disorder, whose causation can be traced. If we can identify the link between the heart and the shoulder joint, perhaps we shall be able to throw some light on the pathogenesis of arthritis due to other causes.

Reflex Nervous Mechanism.

Most observers agree that the periarthritis can be explained only as due to an underlying disturbance of nerves. Spillane and White (1939) and others have seen herpetic eruptions in the area of radiation of *angina pectoris;* and herpes is a neurogenic manifestation—the effect of antidromic nervous stimulation (Lewis, 1937). Shapiro *et alii* hold that the ulceration of the hands described by them is a "trophic" nervous manifestation, due to antidromic nervous stimulation. MacKenzie (1923) and others have described cutaneous hyperalgesia in the field of cardiac radiation, while Gibson has described sensory loss.

The deep tenderness that often accompanies angina is referred or reflex in origin, and some authors have suggested that the fixation of the shoulder joint may be due, in the first place, to reflex spasm of muscles. But reflex spasm will not account for a rheumatic joint lesion with profound muscular wasting. Nor will it explain the swelling of the wrist and hand. The evidence suggests that the shoulder lesion is a "trophic" disorder due to nervous impulses generated by the diseased heart muscle. When it spreads to involve other joints, nervous impulses again play a part. Steinbrocker, Spitzer and Friedman (1948) have described in detail a reflex mechanism—the "shoulder-hand syndrome"—that connects dystrophy of the hand with periarthritis of the shoulder.

Recently I have reported cases of polyarthritis precipitated by injury to a single jojint (Kelly, 1948, 1949). After damage to a joint, arthritic changes appear in other joints, and the symmetrical spread of the disorder suggests that nervous pathways are involved. We should not be surprised, therefore, to find that the periarthritis precipitated by coronary disease may lead to changes in other joints.

Summary.

1. Periarthritis of both shoulders and arthritis of both wrists developed in a patient with myocardial ischæmia.

2. The evidence suggests that the shoulder lesion is generated by nervous reflexes, and that the other joints are involved through the same channels.

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Reviews.

THE PATHOLOGY OF TUMOURS.

THE advent of a new and comprehensive text on neoplasms[1] by such a thorough student and prolific writer of monographs as R. A. Willis will be welcomed in all English-speaking countries, but it is particularly welcomed in this country because the author is an Australian, though now residing and working in England. Ewing's "Neoplastic Diseases" has run into several editions and has been a reference text for a generation, and though in some respects a valuable book, it was not entirely satisfactory. Willis leaves one in little doubt as to his opinion on any subject and this makes attractive reading, though there will be authorities who will not relish his criticism or agree with him.

The book opens with 200 pages on general oncology, classification, malignancy, experimental carcinogenesis, causation, metastasis, and tumours in animals. This is a valuable and interesting résumé of what one should know about tumour growth. Willis is a pessimist on the virus theory and predicts that it will be found that ultra-microscopic parasites are not concerned in the change from normal to neoplastic cells. In view of recent work this is a brave stand for a pathologist to take.

The remaining 750 pages are a systematic account of the tumours of the various organs and tissues. Willis is not in favour of many subgroups of tumours or of grading them for malignancy owing to the variations often found in different parts of the same tumour. The text gives prominence to the main problems confronting the surgical pathologist such as histogenesis, differential diagnosis and malignancy, and is obviously written by one who has studied a large amount of his own material and the published work of many others. It is not possible to traverse or review his treatment of the pathology of the tumours of all the various organs and systems, but some examples may be mentioned.

To the breast he devotes fifty pages, and he deals adequately with the cystic hyperplasias and intraduct and intraacinar carcinoma and justly concludes that hyperplasia is a more common antecedent to infiltrating carcinoma than the 20% figure given by Cheatle and Cutler. The photomicrographs are very well chosen and beautifully produced. Concerning Paget's disease of the nipple, Willis takes up a definite position, as he does on most controversial problems. He believes that the Paget cells in the epidermis represent a carcinomatous or precarcinomatous change in the epidermis and that the carcinomatous changes in the duct epithelium are a concomitant change in a field of tissue including both ducts and epidermis. The photographs of either school produce rather convincing evidence for their respective interpretation. And there the matter must rest for the nonce.

Each section is provided with a good bibliography, the more important papers in larger type.

To take another subject by way of example—Willis gives nineteen pages to the melanomata. He states that the histogenesis has been confused by assuming that they all have a common cell origin whether the theory be an epithelial, mesodermal or nervous origin. But these cells, in various situations and with no close affinity, have but one common character, melanin production. Tumours arising from these different cells in different situations, the skin, the retina and the leptomeninges must be considered separately. He agrees with Dawson and Nicholson that cutaneous moles are of epidermal origin and are not of nervous origin, and further that the compound structure sometimes found is further evidence that they are a cutaneous malformation.

Concerning thyreoid tumours Willis has few doubts. Adenomata of benign structure, but papillary, are for prognostic purposes malignant adenomata. Papillary adenomata cannot be distinguished from papillary carcinomata. Carcinomata arise from preexisting adenomata in a high proportion of cases, probably in the majority. This latter view is appreciated by many surgeons, but not by as many physicians. He agrees with King and Pemberton on the lateral aberrant thyreoid tumours and goes perhaps a little further when he states that in these cases a small carcinoma will always be found in the homolateral lobe. The so-called benign metastasizing goitres are only of historical interest, for adequate examination of metastasizing thyreoid tumours will always reveal ample evidence of carcinoma. A difficulty not mentioned, however, is that the thyreoid gland is not always available for examination. It may present no clinical evidence of tumour. Hürthle-cell tumours arise almost certainly from ordinary thyreoid epithelium and are only one of the many structural variants. Many are benign and do not recur, but some are malignant. He discusses the rare mixed connective tissue and epithelial tumours of the thyreoid, and finds that the metastases are not mixed but sarcomatous.

In nearly all chapters Willis has something interesting to say about corresponding tumours in animals, and particularly in dogs. There is no question but that Willis is frank and downright in his views and not sparing of criticism of others on vital points. But this makes for more piquant reading and all must admit that he is a very through and sound histologist with a wide knowledge of the literature of oncology. This book is a fitting successor to his valuable text on the spread of tumours in the human body which was published some fifteen years ago from Melbourne. His "Pathology of Tumours" is well printed in large and clear type on good paper and is beautifully illustrated. There is no doubt that it should and will be found on every pathologist's bookshelf, and surgeons will find it a valuable book in their consulting rooms. It should also be available for medical students studying their special pathology. Dr. Willis has done a job for Australian medicine of which he may well be proud.

[1] "Pathology of Tumours", by R. A. Willis, D.Sc., M.D., F.R.C.P.; 1948. Sydney and London: Butterworth and Company (Publishers), Limited. St. Louis: The C. V. Mosby Company. 9½" × 6½", pp. 1126, with 500 illustrations.

THE MEDICAL ANNUAL, 1949.

THOSE of our readers who have acquired what we have often called the "Medical Annual habit" and have come to regard the Annual as an essential institution, or better as a friend who calls once a year, will be interested to know that "The Medical Annual, 1949"[1] was printed entirely at the publishers' own works for the first time after an interval of eight years—the interval from the destruction of the publishers' Stonebridge works by enemy action to the completion of a new modern factory. This, the sixty-seventh consecutive issue of "The Medical Annual", maintains the standard of usefulness and attractiveness which its editors, Sir Henry Tidy and Professor Rendle Short, have led us to expect. Apart from the systematic presentation of material judiciously abstracted from current journals and books, certain subjects of particular topical interest are, according to custom, given special treatment by appropriate authoritative contributors. Among such subjects are aureo-

[1] "The Medical Annual: A Year Book of Treatment and Practitioner's Index." Editors: Sir Henry Tidy, K.B.E., M.A., M.D. (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.S., B.Sc., F.R.C.S.; 1949. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 8¼" × 5½", pp. 658, with 79 illustrations.

mycin, "The British Pharmacopœia,1948", the chronic aged sick (a particularly valuable and informative article), surgery of the sympathetic nervous system and vagotomy, prefrontal leucotomy, permanent waving of the hair, the æetiology and treatment of malaria, social medicine (a constructive article by Professor F. A. E. Crew, who recently visited Australia), vital statistics, radiotherapy, and surgical aspects of the treatment of pulmonary tuberculosis, gastric and duodenal ulcer and other diseases of the stomach, coarctation of the aorta, carcinoma of the rectum and parkinsonism. The article on legal decisions and legislation is, as usual, of considerable interest. The volume is well and freely illustrated, a number of the illustrations being in colour, and is completed by the customary index of new preparations and appliances and list of books of the year. There is probably no medical practitioner who would not be better off for having the current volume of this publication appear on his book-shelf each year.

AVIATION MEDICINE.

IN "Aviation Medicine: Its Theory and Application", the latest publication received on this theme, Kenneth Bergin shows that he is a man who knows his subject.[1] With his extensive war and post-war experiences he is well fitted to write such a book and, as he is a pilot also, his views have added authenticity.

This book is a "must" for those interested in this branch of medicine and one which all doctors should read. Particularly valuable to Air Force medical officers are the chapters on aircrew neurosis, flying stress and morale with their wealth of knowledge and sound common sense. These chapters are naturally "Air Force", since such things as flying stress are predominantly service in origin. In civil aviation the problem is harder to get at, and one would have liked to have Bergin's ideas on this angle of things.

A chapter of interest to general practitioners deals with the transport of invalids *et cetera* by air, and includes the table of medical contraindications to air travel which appeared recently in the *British Medical Journal*. The transportation by air of the sick and injured is becoming increasingly popular in Australia, and doctors generally should study the advice which is given here. One would have liked to have more stress placed on the undesirability of transporting badly shocked patients by air. Another useful section deals with health requirements for international travel and includes a table which will be helpful in interpreting smallpox vaccination reactions.

The remainder of the book covers all those diverse and interesting aspects of aviation medicine which are of importance to specialists in this branch of medicine. The book is well produced and the excellent illustrations include coloured photographs of otitic barotrauma and ariboflavinosis. One only wonders whether, as stated on page 211, 40% of people are air-sick on their second flight—the figure would be nearer 4·0% to judge by Australian experiences.

Appendices are (1) I.C.A.O. Medical Requirements (useful for examiners for flying licences); (2) Table of Average Body Build; (3) Epidemiological Maps; (4) International Certificates of Inoculation and Vaccination; (5) Yellow Fever Inoculation Centres in United Kingdom.

HYPERTENSION.

IT is particularly pleasing to be able to read in a small monograph a concise, interesting and very informative account which reviews the present state of our knowledge of hypertension and the experimental work on this very important disease since 1928. Harry Goldblatt has succeeded in producing just such an account in what he calls a "written lecture" on "The Renal Origin of Hypertension".[2]

After an interesting introductory historical summary covering the clinical approach to the problems of hypertension, the various methods hitherto employed in the experimental production of renal hypertension are reviewed prior to a description illustrated by numerous charts of the procedures employed by Goldblatt and his collaborators.

The experimental method of production of constriction of a renal artery is described and then the effects of such are illustrated. A "benign phase" is produced by moderate constriction of both renal arteries and a "malignant phase" of experimental renal hypertension develops after great constriction of both renal arteries. The pathological changes and particularly arteriolar necrosis are described and the pathogenesis is discussed. The humoral mechanism of production of hypertension put forward is that renin, an enzyme from the kidney, acts upon hypertensinogen, a globulin in the blood plasma, to form hypertensin, a polypeptide, which is the active vasoconstrictor substance, and which can be inactivated by hypertensinase, an enzyme present in the blood and in extracts from other organs. The chemical and physiological properties of renin, hypertensinogen, hypertensin and hypertensinase are described. The discussion then passes naturally to the medical and surgical treatment of hypertension. Finally, the similarities and differences between human essential hypertension and experimental renal hypertension are summarized. The only jarring feature in the book is the bad misprint in the title of this last chapter, which is present also in the list of contents.

The work of Wilson and Byrom is dismissed rather summarily with the statement that the change in the contralateral kidney in rats was probably due to bilateral renal disease at the time of the experiment, but it is admitted that the rats may differ from all other animals.

Despite minor slight disadvantages due to brevity, this book can be enthusiastically recommended to all clinicians who are interested in the problems of hypertension.

RADIOACTIVE INDICATORS.

A VOLUME entitled "Radioactive Indicators" has been prepared in the Universities of Copenhagen, Stockholm and California by George Hevesy.[1] The author is known as a Nobel Prize winner; as one of the earliest experimenters with artificial radioactive elements he did much to develop tracer technique.

The volume is an encyclopædic collection of the results of tracer tests which have been used in the study of biochemical, physiological and pathological problems.

The methods of production of individual radioactive indicators in suitable forms are described in the early chapters. Discussion of methods of measuring the activities of radioactive samples follows, and a full description of Geiger-Müller counting chambers, amplifying and scaling units is given.

A detailed study of the absorption, distribution and excretion of elements normally or abnormally present in the body follows, including detailed sections on phosphorus, iodine and iron. Much interesting information about the less important elements and the "trace" metals, cobalt, manganese and copper, is given.

The author records that air-borne products of atomic fission such as radioactive strontium, yttrium, circonium and cerium may all be absorbed by inhalation. All are liable to ultimate deposition in the skeleton, but considerable radiation damage may also occur to the lungs.

A compilation of work on permeability of tissue membranes and barriers makes another full chapter. It is interesting to note that the permeability of the blood-cerebro-spinal fluid barrier is very slow, taking of the order of one hour to reach equilibrium, the evidence suggesting that cerebro-spinal fluid production is a secretory function. Similarly, aqueous humour production is a secretory mechanism; while equilibrium across the placenta between maternal and fœtal circulations takes about six hours. Radioactive sodium was used in all the above tests. Equilibrium between blood and extravascular tissue fluids is reached in contrast within four minutes.

The use of radiophosphorus has allowed most interesting studies of nucleic acid metabolism and it is confirmed that X-radiation of small amounts seriously interferes with nucleic acid production. This effect is probably one of the fundamental biological actions of the ionizing radiations.

Tracer studies with radiosulphur have been used to determine the mode of action of the nitrogen mustards. Mustard reacts with serum proteins, nucleoproteins and

[1] "Aviation Medicine: Its Theory and Application", by Kenneth G. Bergin, M.A., M.D., D.P.H., A.F.R.Ae.S.; 1949. Bristol: John Wright and Sons, Limited. London: Simpkin Marshall (1941), Limited. 8½" × 5½", pp. 648, with 131 illustrations. Price: 35s.

[2] "The Renal Origin of Hypertension", by Harry Goldblatt, M.D., C.M.; Publication Number 14 of the American Lecture Series, edited by Paul R. Cannon, M.D.; 1948. Springfield: Charles C. Thomas. 9" × 5¾", pp. 140, with 38 illustrations. Price: 15s.

[1] Radioactive Indicators: Their Application in Biochemistry, Animal Physiology and Pathology", by George Hevesy; 1948. New York: Interscience Publishers, Incorporated. London: Interscience Publishers, Limited. 9" × 6", pp. 580, with illustrations. Price: $10.00.

keratin, forming stable compounds. Affinity for the nucleic acid systems explains the radiation-like action of the mustards, and the affinity for keratin explains the cutaneous damage caused by mustards.

Phosphorus and calcium metabolism experiments and conclusions are recorded in great detail. Studies of metabolism of phosphorus, calcium and fluorine by tooth structures show that renewal of elements occurs both from blood stream and externally by salivary contact.

The final chapters of the work are devoted to the application of radioactive indicators in the study of physiological problems of red blood corpuscles, and the reader is amazed at the mass of material presented. The volume ends with a note of caution on the limitations of the uses of the radioactive indicators.

Hevesy has produced a monumental work. He has fashioned a vast array of apparently non-related investigations into a coordinated and orderly presentation of biological knowledge. The reader is left rather aghast at the huge amount of new knowledge which has been so quickly accumulated, for research workers have not been slow to adapt to their own uses the new research methods which radioactive tracers have provided. One marvels at the unending story of ingenuity which is unfolded. But the saga is only beginning, and opening before us is a limitless field of scientific endeavour. Hevesy has performed a real service in collecting into one volume such a great array of the new knowledge.

Notes on Books, Current Journals and New Appliances.

LABORATORY TECHNIQUE.

THE purpose of "Laboratory Technique in Biology and Medicine", by E. V. Cowdry, is "to expose in an introductory way the technical opportunities for research".[1] The author feels that the possibilities of improving old techniques, of replacing some of them by new ones and of relying more upon microchemical and physical procedures are not explored as they should be. The book seeks to remedy this by drawing attention to a diversity of methods and ideas without always supplying great detail. In many cases reference is given to a journal or other source which should be consulted. By this means and by the use of an alphabetical arrangement a large amount of specific information is made readily available. The only general discussion is in two short sections at the beginning of the book; one deals with choice of methods, indicating by means of darker type subjects to which further reference should be made in the main part of the book; the other is concerned with standardization of stains and their names. In the second edition, this book has been considerably expanded from its first edition.

ADVANCES IN INTERNAL MEDICINE.

VOLUME III of "Advances in Internal Medicine" consists of a group of separate articles on particular subjects of current interest in which advances have been made.[1] These are respectively BAL, hæmolytic anæmias, factors modifying the therapeutic activity of penicillin, streptomycin in the treatment of tuberculosis, histoplasmosis, the treatment of hyperthyreoidism with antithyreoid compounds, the diagnosis of disease by enzymic methods, plasma fractionation, the mechanism of acclimatization to heat, and modern therapeutic agents used in neurological conditions. Each subject is covered in considerable detail and much recent work is brought together which is otherwise not readily available. A full list of references is given in each case. In addition to an author index and a subject index, a cumulative index is included which covers Volumes I and II as well as the present volume of the series. The printing and layout of the book are attractive, and it should be acceptable and useful to all who are interested in the subjects listed.

[1] "Laboratory Technique in Biology and Medicine", by E. V. Cowdry; Second Edition; 1948. Baltimore: The Williams and Wilkins Company. London: Baillière, Tindall and Cox. 9" × 5¾", pp. 685. Price: 22s.

[1] "Advances in Internal Medicine", edited by William Dock, M.D., and I. Snapper, M.D.; Volume III; 1949. New York: Interscience Publishers, Incorporated. 9" × 6", pp. 498, with a few illustrations. Price: $8.50.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Thyroid Hormones and their Action", by G. Mansfield, M.D.; translated by Erwin Pulay, M.D.; 1949. London: Frederick Muller, Limited. 9½" × 6", pp. 176. Price: 24s.

First published in German at Basle, Switzerland, in 1948, under the title *"Die Hormone der Schilddrüse und ihre Wirkungen"*.

"Bacteriological Technique: A Guide for Medical Laboratory Technicians", by W. W. W. McEwen, A.I.M.L.T., F.R.M.S., with a foreword by Professor Sir Alexander Fleming, F.R.C.P., F.R.C.S., F.R.S.; 1949. London: J. and A. Churchill, Limited. 8" × 5", pp. 308, with 70 illustrations. Price: 15s.

The purpose of the book is set out in its title.

"The Biology of Mental Defects", by Lionel S. Penrose, M.A., M.D., with a preface by Professor J. B. S. Haldane, F.R.S.; 1949. London: Sidgwick and Jackson, Limited. 8½" × 5½", pp. 302. Price: 21s.

A book on primitive human societies and other forms of incomplete human achievement and also a contribution to general culture.

"Roentgen Diagnosis of Diseases of the Skull"; Monographic Atlases; Volume XIX; Annals of Roentgenology; by Max Ritvo, M.D.; 1949. New York: Paul B. Hoeber, Incorporated. 10¼" × 7¾", pp. 436, with 368 illustrations. Price: $6.00.

Both normal appearances and abnormal variations are dealt with in this atlas.

"Recent Advances in Physiology", by W. H. Newton, M.D., M.Sc. (Manchester), D.Sc. (London); Seventh Edition; 1949. London: J. and A. Churchill, Limited. 8" × 5", pp. 280, with 89 illustrations. Price: 21s.

The sixth edition was published in 1939.

"British Red Cross Society First Aid Manual No. 1", by Sir Harold E. Whittingham, K.C.B., K.B.E., F.R.C.P., and Sir Standford Cade, K.B.E., C.B., F.R.C.S.; Ninth Edition; 1949. London: MacMillan and Company, Limited. 6" × 5½", pp. 322, with 171 illustrations. Price: 3s.

The subjects are dealt with in their order of importance as life-saving measures and the frequency with which they are encountered by the first-aides.

"Clinical Diagnosis by Laboratory Examinations", by John A. Kolmer, M.S., M.D., Dr.P.H., Sc.D., LL.D., L.H.D., F.A.C.P.; Second Edition; 1949. New York: Appleton-Century-Crofts, Incorporated. 9½" × 6½", pp. 1244, with 93 illustrations. Price: $12.00.

The primary purpose of the book is to present the clinical interpretations of laboratory examinations and their practical applications in the diagnosis and differential diagnosis of various diseases.

"Physiology in Diseases of the Heart and Lungs", by M. D. Altschule; 1949. Cambridge and Massachusetts: Harvard University Press. 8½" × 5½", pp. 388. Price: $5.00.

Written at the request of third and fourth year students at the Harvard Medical School.

"Vision: Its Development in Infant and Child", by Arnold Gesell, M.D., Frances, L., I.L.G., M.D., and Glenna E. Bulls; 1949. New York: Paul B. Hoeber, Incorporated. 9" × 6", pp. 332, with 72 illustrations. Price: $6.50.

Based on investigations carried out at the Yale Clinic of Child Development.

"The 1949 Year Book of Pediatrics (July, 1948-July, 1949)", edited by Henry G. Poncher, M.D., with the collaboration of Julius B. Richmond, M.D., and Isaac A. Abt, M.D.; 1949. Chicago: The Year Book Publishers, Incorporated. 7" × 4½", pp. 562, with 120 illustrations. Price: $4.50.

One of the Practical Medicine Series of year books.

The Medical Journal of Australia

SATURDAY, JANUARY 28, 1950.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

CHILD HEALTH.

REFERENCE was made in these columns a week or two ago to the recent appointment at the University of Sydney of a Professor of Child Health and to the steps which had preceded it. Attention was drawn to the title of the chair—it is not a chair of diseases of children or of pædiatrics, but has a wider significance. It is essential that this significance should be recognized by medical practitioners and indeed by all who have to do with medical education and practice throughout the length and breadth of the Australian continent, for on this understanding the success of the chair and possibly its duplication in other places will largely depend. The term "child health" was used in what has become known as the Goodenough Report on Medical Schools, issued in 1944. It was used as the heading to a chapter dealing with the training of medical students in the health and diseases of children from birth onwards. The term pædiatrics is becoming more and more widely used as descriptive of this branch of medicine, and those who practise it are, of course, known as pædiatricians. If we look at the derivation of the word pædiatrics, we find that it is a less wide term than child health, for it comes from the Greek παῖς, a boy, and ἰατρός, a physician. However, though it will be well to insist that the chair is a chair of child health, as laying chief emphasis on health rather than on disease, there is no need to clamour for any terms other than pædiatrics and pædiatrician for general use. Students of pædiatrics, like those who study general medicine, know that prevention of disease is more important than its cure and those with real discernment act in accordance with this knowledge. Pædiatrics is different from other specialties in medicine. It is, as is pointed out in the British Medical Association's report of 1948 on medical education, general medicine applied to a particular age period. It is described as a horizontal section of medicine, as distinct from the vertical divisions formed by some other specialties—"pædiatrics comes into contact, like general medicine itself, with many different branches of practice, including social medicine, psychiatry, orthopædics and infectious diseases". This was expressed in another way at a symposium on undergraduate education in pædiatrics at the annual meeting of the American Pediatric Society in May, 1947.[1] Irvine McQuarrie described pædiatrics as "that division of medical science and practice which deals with all aspects of the physical, mental and emotional health of the human race throughout infancy, childhood and adolescence". He laid emphasis on the fact that pædiatrics is concerned with the whole person and that the person concerned is undergoing continuous developmental change. Since pædiatrics is such a fundamental and comprehensive subject, there can be no disagreement with the contention that undergraduate and graduate teaching in the subject should be soundly planned. We do not need to be reminded that a large part of the practice of every general practitioner is concerned with children, but it may not be constantly realized that the protection of child life is essential to the welfare and the future of the community. The medical profession points with pride to the low infantile mortality rate of which most modern countries can boast today. We know that preventive medicine and the insistence on practical hygiene have been largely responsible and we know also that it is in the years of infancy and childhood that much of the advance has been achieved. This must not be allowed to lead to a complacent attitude—there is always room for further advance. Only recently there has been recorded in these columns the satisfactory state of the nutrition of the poorer people in Britain, because of the equitable distribution of food. No one can say with truth that all is well with the preventive practice of pædiatrics, in other words, with the maintenance of child health, if social status is *per se* a deterrent.

There are some aspects of pædiatric teaching and training of which we do well to remind ourselves. In the British Medical Association report on education it was pointed out that there are several ways in which pædiatrics contributes to the training of a good doctor. First of all, more than any other part of the medical course, it helps to stress the preventive aspect of medicine, "for pædiatrics includes in its scope the physical, mental and spiritual care of the child both in health and in disease, a charge fraught with great possibilities for good or for evil in childhood and adult life". Secondly, when he deals with children, the student is made to realize in a special way the value of history-taking and the need for careful clinical examination. Thirdly—and too much stress cannot be laid on this—no other part of the medical course serves so well to stimulate the personal qualities of patience, gentleness and kindness to the patient, which go to make the good doctor. The next point that arises is the kind of training which the undergraduate student should receive in the subject. Remembering our definitions, we shall have no trouble in placing health first and disease last, but it will be useful to refer to the Goodenough Report. Here it is stated that the teaching of pædiatrics can best be developed along the lines that child health and children's diseases constitute an important part of the training in general medicine and to a lesser extent in surgery, and that, in addition to a relatively short period devoted to intensive training in the subject, teaching on the health and disease of children should run "like a golden thread" through the whole curriculum. The statement is made that the student should be brought into

[1] *American Journal of Diseases of Children*, November, 1948.

touch as much as possible with healthy children. The recommendation is that the intensive part of the undergraduate course should include instruction and practical experience in: (*a*) the care and management of newborn infants; (*b*) the nutrition and development of normal healthy children; and (*c*) the diseases of children. When this logical sequence of study is adopted, the set lecture, if it survives at all, will be more of a lecture-demonstration; it will not be like the infliction suffered years ago by certain older graduates, when diagrams and dogmatic statements, delivered with dignity and conviction, nevertheless seldom aroused a lively interest. To draft a syllabus of lecture-demonstrations for large numbers of students will not be easy, but would probably be dependent on the arrangement of clinical clerkships in pædiatric hospitals. This is a branch of the subject which almost calls for a separate discussion. The General Medical Council in Great Britain recommended a period of clerkship of not less than one month's duration. With this we agree. According to the Goodenough Report the British Pædiatric Association advocated that the period of clerkship should last for three months and be full time. However desirable this might be, most medical education experts will declare it to be impossible as conditions are at present. At the same time it may be noted that at the American symposium W. C. Davison, of the Duke University School of Medicine, advocated an undergraduate schedule of training in pædiatrics which "should contain a solid block of three months in the wards and in the clinics during the senior year".

In the present discussion only the fringe of an important subject has been touched. No reference, for example, has been made to post-graduate teaching of child health, and we shall all agree that much might be written on that subject. When W. C. Davison can declare to a meeting of the American Pediatric Society that no medical school has a completely satisfactory answer to the question of adequate undergraduate and post-graduate pædiatric education, there is reason to ask Australian practitioners to inquire whether all is being done in this country that can be done under present conditions.

Current Comment.

DEOXYCORTONE AND RHEUMATOID ARTHRITIS.

THE use of hypophyseal and adrenal cortical hormones in the treatment of rheumatoid arthritis has attracted much recent attention, the highlight being, of course, cortisone or compound E. Further interesting possibilities are suggested by a preliminary report of work carried out in Sweden by E. Lewin and E. Wassén.[1] Nine patients with rheumatic disease of the joints were treated with an intramuscular injection of five milligrammes of deoxycortone acetate in one millilitre of *Oleum Arachis*, immediately followed by an intravenous injection of one gramme of ascorbic acid (10 millilitres of a 10% solution). According to the report all the patients reacted similarly. Five minutes after the injections the articular pain began to diminish and the articular mobility began to increase. Fifteen to thirty minutes later, the pain had practically disappeared and the mobility improved as much as the anatomical changes in the joints and muscular atrophy would allow. One patient, completely crippled by pain and contracture after rheumatoid arthritis for fifteen years, sat up with ease, it is stated, after one combined injection and moved her arms and legs about freely; all her pain had gone. The effect lasted from two to six hours, occasionally more than twenty-four hours, and the impression was that it lasted longer with each further injection. The most suitable dosage and other details of administration are still being considered. No toxic side-effects have been observed, though it must be constantly borne in mind that deoxycortone acetate is not an innocuous substance.

The dramatic results claimed by Lewin and Wassén are so rapid that it should not take long for them to be substantiated or otherwise by other workers. Already a correspondence has developed in *The Lancet*, with a notable discrepancy between results in individual preliminary reports. J. H. Kellgren,[1] of the Rheumatism Research Centre at the University of Manchester, has observed no beneficial results from the combined injection and considers the Swedish claims "most unfortunate". Separate reports from D. LeVay and G. E. Loxton and from W. W. Fox[2] contain results quite as dramatic as those of Lewin and Wassén, though not so consistently produced. Fox suggests that Kellgren's patients, who were all in hospital, had already made the maximum possible improvement; Fox's patients were ambulatory and unable to take proper rest or have other adequate treatment. Preliminary trials by S. J. Hartfall and R. Harris and by V. L. Hart and F. Storer[3] offer no support for the Swedish claims, though Hart and Storer noted the occurrence of temporary euphoria, which may, they suggest, account for such favourable effects as they observed. With the two last-mentioned reports is published a letter by Loxton and LeVay, who stress the importance of correct technique so that the two substances may both be available in satisfactory concentration at the appropriate time. The most recent report is by T. D. Spies, R. E. Stone, E. D. Maeyer and W. Niedermeier,[4] who had been investigating the treatment of rheumatoid arthritis with injections of deoxycortone acetate and ascorbic acid, given to patients restricted to a diet of low sodium content, when Lewin and Wassén's report appeared. Spies *et alii* had observed no benefit up to that time, but continued their observations with the Swedish work in mind; they were still unable to obtain amelioration of symptoms. They then divided their six patients into two groups. The dietetic restrictions and the injections of deoxycortone acetate were continued, the administration of ascorbic acid was ceased; three patients were given injections of adrenocorticotropic hormone and three were given injections of distilled water. The adrenocorticotropic hormone produced prompt relief, which continued while the injections continued, relapse following their cessation. This is the type of response which has now come to be expected since Hench *et alii* introduced the treatment. It seems that Lewin and Wassén's claims for a comparable response from deoxycortone acetate and acetic acid have not yet been established. Even if this is not achieved, further investigation is important; there must be some reason for the benefits claimed by them and by others. Meantime their régime of treatment is not one that can be safely followed by those not fully conversant with therapy of this type.

[1] *The Lancet*, November 26, 1949.

"PLEURAL SHOCK."

A WELL-ESTABLISHED idea in medicine often dies hard even though its validity has been successfully challenged. Terms expressing such ideas can be even more persistent. One such term, which according to Andrew Morland[5] should be dropped, is "pleural shock". Morland, who is physician in charge of the tuberculosis department at University College Hospital, London, has had extensive clinical

[1] *Ibidem*, December 10, 1949.
[2] *Ibidem*, December 17, 1949.
[3] *Ibidem*, December 24, 1949.
[4] *Ibidem*, December 31, 1949.
[5] *The Lancet*, December 3, 1949.

experience of procedures involving pleural puncture, and he feels that the concept of "pleural shock", originating in Roger's original description in 1864, has outlived its usefulness and the term itself is misleading; "there is no evidence that mechanical or chemical stimulation of sensory nerves in the pleura is any more likely to produce serious or fatal accidents than similar trauma in other parts of the body". As a corollary to this and in conformity with his own clinical experience, Morland asserts that, provided an adequate collapse of the lung has already been obtained, there is no reason to believe that local anæsthesia increases the safety of a pneumothorax refill; nor has he found any advantage (but rather the contrary) from local anæsthesia in the reduction of pain associated with the operation. Accumulating experience of many clinicians and experimenters has shown that air embolism, either cerebral or coronary, is the commonest cause of accidents accompanying refills. The cerebral accidents are usually fairly obvious; the coronary accidents are more subtle, and offer an explanation for many of the cases in which the concept of pleural shock has persisted. The immediate source of the air is not necessarily external, and Morland stresses the point that when difficulty is experienced in finding the pleural space, the patient should not be encouraged to breathe deeply, since this may lead to the passage of air into a pulmonary vein directly from air-containing tissue, even when no air is given from the pneumothorax apparatus. This is more likely to occur when lung tissue is indurated by chronic inflammation; the veins are held open, and a needle may well make an opening between airway and vein through which air may be sucked. That puncture of a healthy area of lung is unlikely to cause air embolism is illustrated by the rather startling case of the patient who had weekly refills of 1000 millilitres of air from an enthusiastic but inexperienced practitioner for a year with typical intrapulmonary pressure readings and no radiological evidence of air in the pleural cavity; the absence of ill effects was "possibly due to the fact that the lung was perfectly healthy, the hæmoptysis for which the pneumothorax was attempted being due to a dry bronchiectasis on the other side".

Other causes of syncope during paracentesis of the pleura need to be remembered. Morland refers to the people who lose consciousness on receiving a hypodermic injection, to the moribund who are susceptible to various minor interventions, and to the rare cases, sometimes designated as *status lymphaticus*, in which a trivial operation causes death. These offer no particular support to the idea of pleural shock as an entity. From twenty-five years' experience Morland has been able to collect only five cases of serious accident associated with paracentesis of the pleura, an incidence of 1:10,000, but these have some interesting features. He presents the clinical history of each. Air embolism was apparently not the cause of these accidents, the evidence suggesting that disturbance of the heart from reduction of the intrathoracic pressure was the most likely explanation. This cannot be thought of as a common cause of mishap, but since such accidents are most likely to happen when the pleura is thickened and inelastic, it is important in such cases to avoid very low pressures during aspiration or replacement of fluid.

TETANUS INFECTION IN HOSPITAL.

THE infection of a patient with tetanus while in hospital is the type of catastrophe which should never occur. Fortunately it very rarely does, but full information relating to those rare occasions should be made known widely, so that others may check on possible chinks in their antiseptic armour. A Canadian report on plaster of Paris as a source of infection with tetanus and gas gangrene was mentioned in these columns on April 23, 1949, and several years ago (December 28, 1946) we referred to the death of babies in New Zealand from tetanus originating in talc used for routine toilet purposes; these last-mentioned infections did not occur in hospital, but are in many respects in the same class. The latest report, by S. Sevitt,[1] contains certain other features which may well be noted. Two patients who had received surgical treatment in the same hospital developed tetanus in May, 1949. The operations had been carried out in an operating theatre which was one of two in a suite connected by a central assembly room with the usual annexes. Building repairs were in progress in the second theatre, the assembly room and the annexes. Repairs in the theatre used had been completed a few weeks previously. Among the building materials was a considerable quantity of animal hair which the plasterers beat with laths on a table before mixing it with plaster, in which it acted as a binding material. This hair, which further inquiries indicated probably came from goat skins of Abyssinian origin, produced on culture a heavy growth of various strains of anaerobic sporing bacilli, including toxigenic strains of *Clostridium tetani*; some of the other strains produced muscle gangrene experimentally in guinea-pigs. The evidence points to this hair as the original source of the tetanus infection. From dust or floor sweepings of various parts of the theatre suite and from specimens of talc used as glove powder, toxigenic strains of tetanus and other anaerobic sporing bacteria were isolated. This is thought to have been the result of dissemination of spore-containing dust originally contaminated from the plaster-hair. The dissemination was probably brought about by cross-currents of air in the theatre, produced by the exhaust ventilation system. Samples of sterilized silk sutures and cotton wool and swabs from autoclaved rubber gloves failed to yield any organisms. Clostridial strains, including toxigenic *Clostridium tetani*, were isolated from talc autoclaved at 20 pounds' pressure and ready for use. This imperfect sterilization was considered to have arisen from the tight packing of the powder packets and was verified experimentally. The contaminated glove powder was probably the final vehicle whereby tetanus spores reached the patients' wounds. In a constructive discussion of the incident, Sevitt refers to the three agents in the probable chain of infection: the plaster-hair, the cross-currents due to the ventilation system and the talc. He points out the desirability of having operating theatres equipped with the forced-ventilation type of air-conditioning system designed to ensure an atmosphere almost free from bacteria to begin with and to cause rapid evacuation of organisms disseminated through the air in the course of dressings and the like. He suggests that opposition to the general installation of such plants on the grounds of expense is reminiscent of the attitude taken in Lister's time in relation to expensive sterilizing equipment. The principle of his recommendations is certainly right, though opinions will differ on the validity, at any rate in degree, of his Listerian comparison. With regard to talc, Sevitt recommends, first, that it should be packed in small quantities for sterilization, and that the packets should be well separated from one another in the drum container; this will allow the easy removal of air during the autoclaving and the easy entry and circulation of superheated steam. Secondly, non-sterile talc should not be used to dust rubber gloves, mackintoshes *et cetera*, since these are normally autoclaved at only five pounds' pressure to prolong their life; the dusting should be performed with talcum powder which has already been autoclaved at 20 pounds' pressure. Finally, the efficiency of autoclaving should be bacteriologically controlled with a selected suspension of *Bacterium subtilis*, in the most tightly packed drums. These measures appear to be common sense and should command general approval. On the first and most important link in the chain, the proximity to major surgical operations of vigorous and untidy plastering activity, and in particular of quantities of plaster-hair, Sevitt makes little comment. Perhaps little could be added to his simple, almost naïve statement: ". . . had this hair not been admitted to the theatre tetanus spores would probably not have been isolated from the other sources." The principle involved is obvious.

[1] *The Lancet*, December 10, 1949.

Abstracts from Medical Literature.

BACTERIOLOGY AND IMMUNOLOGY.

Type Specific Protein from Pneumococcus.

R. AUSTRIAN AND C. M. MACLEOD (*The Journal of Experimental Medicine*, April, 1949) have made a study of a type-specific protein from the pneumococcus. While recognizing the specificity of the capsular carbohydrate substances, the authors thought it useful to apply the Lancefield techniques in modified form to cultures of pneumococci and to search for alcohol-soluble protein fractions such as can be found in hæmolytic streptococci of Group A. They were successful in isolating "M" protein from several different types of pneumococci. They encountered differences of "M" protein in strains of the same type, in both types I and II, showing that organisms possessing similar capsular carbohydrate may have dissimilar "M" protein. Suggestions are made for the naming of organisms in which this difference has been recognized, and the authors suggest that the study of the "M" protein may be a tool useful in the study of the epidemiological variations in behaviour of type strains of pneumococci.

Mouse Pox.

FRANK FENNER (*The Journal of Pathology and Bacteriology*, October, 1948) has studied the clinical features and pathogenesis of mouse pox. He states that this naturally occurring exanthematous condition of mice is closely allied to vaccinia. Virus multiplication of spread was followed in large numbers of mice, titrations being made to estimate the number of infective particles in dilutions of tissue emulsions, the chorio-allantoic membrane or the intraperitoneal inoculation of mice being used, according to whether the concentration was high or low. The initiation of infection in the herd was made by introducing infected animals and watching the development of primary lesions of the skin through minute areas of trauma about the head; this occurred usually about the seventh day. Swelling took place, and a scab formed, which fell off after fourteen days, leaving a permanent scar. Inclusion bodies were demonstrable at the height of this local lesion. A secondary rash developed, usually forty-eight hours after the primary lesion, but severely ill animals often died without the occurrence of the rash. Lesions in the conjunctiva were also present. In the experimentally infected animal, the inoculum having been injected into the pad of the hind foot, virus multiplied locally, then invaded the draining lymphatic glands, and was found four days later in the spleen, on the fifth day in the blood and on the sixth day in the skin. The amount of virus in the spleen was large, and this site was considered to be the origin of the virus in the blood. Both lost their virus content rapidly as the titre of circulating antibody rose. In the skin the virus persisted in decreasing amounts from the sixth to the eighteenth day and was presumably blood-borne from the depot in the spleen. Tests for the presence of antibody showed that this first appeared on the seventh day after infection. Attempts were made to test the role of hypersensitivity in the development of skin lesions by giving mice small doses of a less invasive strain of ectromelia before the test dose, but no evidence was obtained to suggest that allergy played any part in producing a skin reaction to the virus. The author discusses the application of this carefully planned study to the development of infectious diseases in humans, and postulates a close similarity between those diseases having a low incubation period with the spread of virus in mouse pox.

Nucleic Acids and Antibody Formation.

W. E. EHRICH, D. L. DRABKIN AND C. FORMAN (*The Journal of Experimental Medicine*, August, 1949) studied the nucleic acids in the production of antibody by plasma cells. They used an extension of the technique of injecting typhoid vaccine into the pads of rabbits' feet and observing the efferent lymph in the vessel from the popliteal lymph node used in the quantitative study of antibody formation; they studied the nucleic acids of the lymph both by chemical analysis and by histological examination of tissues stained with pyronine, which demonstrates the presence of ribose nucleic acid, or with methyl or malachite green, which shows the presence of desoxyribose nucleic acid. The combination of these methods showed that the amount of desoxyribose nucleic acid increased early, and paralleled the increase in weight of the gland in the first three days, while the ribonucleic acid increased in amount on the fourth to the sixth day after injection. Examination of the histological sections showed that in the early stage the cellular element increasing was the plasma cells, and these contained the ribonucleic acid. The lymphocytes began to increase considerably in numbers only after the ribose nucleic acid and the antibody contents had passed their peak. These results were interpreted as indicating that the plasma cell and not the lymphocyte is responsible for antibody formation.

Ætiology of Pneumonia.

E. S. MAXWELL, T. G. WARD AND T. E. VAN METRE, JUNIOR (*The Journal of Clinical Investigation*, March, 1949), have studied the relation of influenza virus and bacteria in the ætiology of pneumonia. They made attempts to isolate virus from sputum in 69 cases of bacterial pneumonia over a period of nine months, which included two months during which influenza A was known to be prevalent in the community. This period was treated separately in the analysis of results, and was called the epidemic period. Serological studies were made on acute and convalescent serum, and in some cases on serum obtained five months later. Autopsy material, consisting of portions of lung tissue and bronchus, was also tested for virus; here the groups could be separated into those from patients dying of primary pneumonia, those in which pneumonia was secondary to some other disease, and those with no evidence of lung disease. The results were found to be fairly clear cut. During the epidemic period, 17 of 36 patients with pneumococcal pneumonia showed either presence of virus or serological titres indicative of virus infection; 13 strains of virus isolated were similar to virus isolated from uncomplicated influenza infections in the community. During the interepidemic period virus was isolated only once from sputum, and no serological evidence of any kind was obtained that the 33 bacterial pneumonia patients also had virus infections. The virus isolated during this period was a B strain. Among 87 autopsy specimens examined, virus was obtained twice in fatal cases of primary pneumonia, and twice in cases of secondary pneumonia. In three of these instances, no bacterial pathogen was identified; in the fourth a pneumococcus type XI was isolated before death, and the virus proved to be strain B. These all occurred during the interepidemic period. The authors discuss the aspects of concurrent disease and their possible relationship, and the likelihood that the virus may possibly be concerned in an ætiological role.

Surface Phagocytosis and Pneumococcus Type III.

W. BARRY WOOD, JUNIOR, AND MARY R. SMITH (*The Journal of Experimental Medicine*, July, 1949) have continued their studies in surface phagocytosis by examining the inhibition of surface phagocytosis by the capsular slime layer of pneumococcus type III. This organism, remarkable for the wide capsule it possesses in young cultures, can be stained with methylene blue to demonstrate the age of the capsule, or this can be shown by the electron microscope. When phagocytic tests such as produce ingestion of the type I pneumococcus are carried out with type III, no phagocytosis results. Removal of the slime layer, by aging of the culture or treatment with alkali or heat, renders the organism susceptible to surface phagocytosis, and the organisms are destroyed even in the absence of antibody.

Experimental Air-Borne Influenza in Mice.

CLAYTON G. LOOSLI (*The Journal of Infectious Diseases*, March-April, 1949) has studied the pathogenesis and pathology of experimental air-borne influenza virus A infections in mice. An apparatus previously described was used to nebulize suspensions of virus-infected lung in dilutions known to be sublethal. Three groups of 50 mice were treated, and lots of five mice were killed at increasing intervals after exposure, to follow the development of the pulmonary lesions. Special precautions were taken to obtain good fixation of lungs and trachea, and whole lungs were used to make histological preparations and stained by two different techniques. Culture of some lungs in broth was carried out by the pour-plate method; all were found to be bacteriologically sterile. Heads of some mice were also fixed and examined histologically, and serum from some animals was used for virus neutralization tests to establish the specificity of the process. The gross appearance of the lesion began forty-eight hours after inhalation of virus, with pinpoint dark red areas which grew larger and coalesced to produce deep red consolidated areas. Some animals survived in groups, where 80% of the total lung had been affected. In these cases the end of the process produced

greyish atelectatic areas. Study of the histological preparations showed that in comparison with the normal lung the earliest change is in the bronchial epithelium, where there is a change in the cytoplasm and the amount of basophilic material present. There are migrating leucocytes, and by the end of forty-eight hours these appearances increase to actual focal inflammation with congested capillaries, many leucocytes in alveoli and bronchi, and increase in degenerative changes in bronchial epithelial cells and in basophilic cytoplasmic material (which the author interprets as actual virus material). After seventy-two hours, changes are further advanced; many bronchi appear to be denuded of epithelium, and the alveolar spaces are filled with œdema fluid and leucocytes. After four to six days there is still no sign of regeneration of epithelium, many alveoli are collapsed, and the lung is less in volume. After seven days areas of young epithelial cells showing mitosis appear, and these continue, with a change from polymorphonuclear leucocytes to lymphocytes and monocytes in the exudate. In the alveolar septa and in some air spaces, fibrosis is beginning; some alveoli are fully expanded, others are collapsed, so that wide spaces are apparent. These changes continue and persist up to three months after infection, so that chronic changes may be seen side by side with normal tissue. Studies of the sections of the upper respiratory passages in the head showed no lesions comparable with those in the trachea and lungs. The author expresses the opinion that the degeneration of the epithelial cell is achieved to shed the portion of the cytoplasm containing the cytoplasmic material which he regards as virus, and that these altered cells then develop a type of squamous metaplasia and grow peripherally into the collapsed alveoli.

HYGIENE.

Transmission of Salmonella Enteritidis by Rat Fleas.

C. ESKEY, F. PRINCE AND F. FULLER (*Public Health Reports*, July 29, 1949), when investigating flea fæces to determine the presence of plague infection, noticed that a number of fleas were excreting *Salmonella enteritidis*. By further investigation and experiment they were able to show that the two common rat fleas *Xenopsylla cheopis* and *Nosopsyllus fasciatus* may be infected with *Salmonella enteritidis* when feeding on infected mice and that the fleas may transmit the infection from one mouse to another by their bites. Furthermore, the fæces of infected fleas also contain viable organisms in large numbers and provide an additional means by which the infection may be spread. Many fleas become free of the infection, but over half remain infected until death. *Salmonella enteritidis* infection appears to produce certain pathological conditions in the alimentary canal of fleas that tend to shorten their lives. However, some survived the infection for more than two months. The mechanism by which the flea infects its host by its bite is unknown, but probably results from the regurgitation of infectious material from the œsophagus. *Salmonella enteritidis* is one of the agents responsible for the outbreaks of acute gastro-enteritis characteristic of so-called food poisoning diseases. Various factors, such as diseased meat and food contaminated by unsanitary conditions, including the infected fæces of rats and mice, are generally considered the sources of human infection. These experimental transmissions indicate that human infection can be contracted from the bite of the fleas found on rats, or infected flea fæces may contaminate food.

Public Health in Japan.

BRIGADIER-GENERAL C. F. SAMS (*The Journal of the American Medical Association*, October 22, 1949) discusses medical care aspects of public health and welfare in Japan. He states that some progress has been made in preventing widespread disease and unrest, and that a sound organization has been established from the national to the local level, integrating the four fundamentals of preventive medicine, medical care, welfare and social security. Major reforms and programmes which have been undertaken in the fields of preventive medicine and medical care are briefly outlined. The author states that an organizational framework, or blueprint, has been established in these fields, but that the largest part of the problem is still ahead. The problem is one of advice, guidance and training. A great gap in professional knowledge has to be bridged, and until an adequate number of Japanese can be trained in modern knowledge in the fields of health and welfare, continued assistance will be required.

Prophylaxis of Whooping-Cough.

M. J. FOX AND R. SNARTEMO (*American Journal of Diseases of Children*, November, 1949) state that whooping-cough continues to be an important cause of death in infancy. Approximately half of the deaths from whooping-cough occur in infants who have not reached the age at which immunization programmes become operative. Several studies relating to early active and passive immunization are reviewed. The authors believe that an immunization programme can and should be a flexible weapon to be used according to the demands of the situation. The need for protection is directly proportional to the expected exposure. Immunization in the sixth month may be adequate in the most regulated environments, while increasingly earlier protection, extending even from the day of birth, is necessary as the environment becomes less protective. Local statistics of incidence and mortality offer a useful guide to the time when immunization should be performed.

The Infectiousness of Poliomyelitis.

N. SILVERTHORNE *et alii* (*The Canadian Medical Association Journal*, September, 1949) discuss some aspects of a combined field and laboratory investigation into the behaviour of poliomyelitis in a farming area in Ontario. Poliomyelitis virus was isolated in seven out of sixteen cases in which stools were collected within three weeks of the onset of symptoms. In two cases the virus was isolated from the stools of patients with minor illness. In every case careful inquiries were made to trace the possible source of infection, and the findings suggested that the disease was chiefly spread by close contact between children. In most instances patients gave a history of playing with another infected child and having prolonged contact. The infectious period extended from eight days before the onset of symptoms to eleven days after. The authors consider that the child suffering from a minor illness plays a most important role in the spread of poliomyelitis. The incidence of clinical poliomyelitis in the families of patients in 25 primary cases was investigated; none of the 52 adults became ill, and three of the 55 children; this gives a secondary attack rate of 2·8% among family members. In three cases, children attended school in the infectious period immediately before the onset of symptoms; of the total 112 contacts of these children, probably only one developed clinical poliomyelitis.

Dental Caries of the School Child.

K. A. EASLICK (*American Journal of Public Health and The Nation's Health*, August, 1949) discusses the contribution that dentistry can make to a school child's health, presents the mechanism of the caries process, and outlines the six factors essential for caries—a susceptible patient, acid-soluble tooth enamel, acidogenic bacteria, carbohydrate substrate, a specialized enzyme system and the bacterial plague. He reviews a number of the control techniques which research workers are testing for interference with each of these factors. He considers that there is a considerable body of evidence to indicate the validity of control measures of the topical application of sodium fluoride solution and the restriction of fermentable carbohydrates for short periods in children's diets. There is also excellent presumptive evidence to anticipate that both the liberation of one part per million of fluoride in communal drinking waters and the daily use of a combination of an ammonium-liberating dentifrice with a carbamide mouthwash will be developed as routine caries-control techniques for children.

Epidemiology of Streptococcal Infection.

MORTON HAMBURGER, JUNIOR, H. M. LEMON AND R. F. PLATZER (*The American Journal of Hygiene*, March, 1949) studied the significance of nose to throat carrier ratios in the epidemiology of hæmolytic streptococcal infection. Observations were made during 1944 in army hospital wards and training camps, in some of which streptococcal disease was practically absent and in some of which its incidence was high. Further observations were carried out on recruits during 1946. Previous work had shown that when the proportion of nasal carriers of hæmolytic streptococci dispensing organisms into the atmosphere increased, so that the ratio of nasal to throat carriers approximated unity, it would be likely that cases of infection would be more frequent, and this positive correlation was obtained in the present study. In the unit with the lowest attack rate, the ratio was also low—one nasal carrier to 43·8 throat carriers. In the unit in which the attack rate was 31%, there was one nasal carrier to 1·3 throat carriers—the evidence again confirming the belief that the nasal carrier is the dangerous carrier of hæmolytic streptococci.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at Broughton Hall Psychiatric Clinic, Leichhardt, New South Wales, on November 17, 1949. The meeting took the form of a series of clinical demonstrations arranged by the medical superintendent, DR. GUY LAWRANCE. Part of this report appeared in the issue of January 7, 1950.

Hysteria.

Before presenting a group of patients with hysteria, Dr. Lawrance explained that that condition was a psychoneurosis showing an unconscious production of mental and physical symptoms by which the patient could free himself from some present difficulty, or by which he could gain some advantage—real or unreal. Freud claimed that the symptoms of hysteria were due to traumatic experiences, and that those psychical traumata were related to the patient's sexual life. The particular sexual trauma must occur in early life, before puberty, and must consist in actual excitation of the genital organs (coitus-like processes). He doubted whether sex injury after the age of eight years, or ten years at the most, could evoke repression in the absence of previous experiences of the same kind. The repression of the facts of the sexual trauma with all the great energy attached was complete until later on, when perhaps the censor was weakened and the memories of the incident came into consciousness and, in disguised form, constituted the symptoms. The energy of the repressed emotion attached to the incident was thus changed into the energy of the symptom, and was said to be converted, hence the term "conversion hysteria". An unresolved Œdipus complex as a basis had also come to be accepted. The symptoms might be mental or physical: a few of the former were seen in narcolepsy, fugue and somnambulism, amnesia, stupor, double personality and the Ganser syndrome; sensory, motor and visceral symptoms were very common.

Hysteria with Intermittent Amnesia (Fugues), Amblyopia and Dysgraphia.

The first patient in this group was a male, aged twenty-seven years, a motor engineer, and the third child of four. His father was an executive officer in a public organization. His heredity contained no abnormality. The patient had always been somewhat difficult as a child; he was always punished more than the other children. He was a good scholar and passed the intermediate examination without difficulty. At the age of seventeen years, he joined the Australian Imperial Force, and was discharged with the rank of sergeant in 1945 because of war neurosis. For that he received treatment in the psychiatric section at Kenmore Military Hospital and on discharge from there was free of symptoms. Since his discharge from the army, he had been subject to attacks of amnesia, during which he disappeared from home and stayed away for several days and, on one occasion, three weeks. He had no recollection of what had happened to him during those episodes. On one occasion he was picked up by the police in Adelaide, well dressed and nourished, with money in his pockets. He could not explain how and when he arrived in Adelaide and what he was doing there. His last amnesic attack was eleven months before the meeting. On that occasion he took a wireless set and cigarettes from people unknown to him, and left them on the road. He could not explain to the police why or from where he took the articles. There was no charge laid against him. In 1948 he was admitted to Morisset Mental Hospital after a suicide attempt with sleeping tablets. He could not give an adequate reason for his action. For the nine months prior to the meeting he had been employed as a storeman assistant at the Royal Prince Alfred Hospital. Lately his conduct had become erratic, and he had complained of intermittent attacks of loss of vision, in one of which he walked off a railway platform and hurt his face slightly. He had been examined by several ophthalmologists, who reported no ocular abnormality. For some time his handwriting had periodically changed its usual character, so that it resembled that of a seven or eight years old child. Usually after days, sometimes weeks, his handwriting became normal. On his admission to Broughton Hall he appeared perfectly clear and able to give a good account of his past life, except for the amnesic periods. Physical examination of all systems revealed no abnormality. He scored well in the Wechsler-Bellevue test; his intelligence quotient was 116. During his stay in Broughton Hall he had had loss of vision on only one occasion. He reported to the nurse that his vision had totally disappeared, and was anxious to demonstrate the fact to the medical officer in charge of the ward. By the time of the medical officer's arrival he had regained full visual power. In the ward he was rather pressed with activity and lacking in discipline. The clinical diagnosis was hysteria in an inadequate personality. Exploration into the psychogenesis of his symptoms revealed an unhappy marital situation, his wife being sexually non-cooperative because of fear of pregnancy and economic insecurity. It was quite possible that during the fugues he established temporary extramarital attachments. He was not aware of them, though he admitted that on several occasions he had been recognized on the street by women who claimed that they knew him well.

Hysteria with Muscle Spasms.

The next patient, a single woman, aged twenty-seven years, an invalid pensioner, had been admitted to Broughton Hall on September 26, 1949. She was the youngest of three siblings, and had been a delicate child; an attack of pneumonia at the age of seven years had been followed by listlessness and despondency. Her education was poor because school was three miles away and she could not walk the distance; she had correspondence tuition. She was always highly strung and over-quick in her actions. She became a casual domestic aid, but never worked continuously. At the age of eighteen years, she ran into a clothes line, and shortly afterwards developed facial tics, which gave way to throwing about of an arm or a leg; there was associated pain in the limbs. With such a beginning she had reached the present condition, when she jerked the whole body and threw back the head as if trying to avoid the clothes line. She had a very unsteady gait, and had done no work for a good many months. She lived at home and slept in bed with her mother. If she walked quickly the gait was very fair, but if she went slowly, a mild "scissors leg" developed and she appeared to walk as if on springs. Her head was jerking very violently. She was mentally clear, but was not of very high intellectual grade. It was noticed that any excitement made the movements worse, but they disappeared during sleep. Investigation of the family background showed that the father died at the age of sixty-one years of heart disease, and that her mother suffered from asthma and bronchitis. Her two siblings were well.

Dr. Lawrance commented that it seemed that the patient's tonsils had been removed when she was aged seven years, and she developed pneumonia afterwards. Ever since then she had been regarded as a very delicate child, and the mother still pampered her even to the point of sleeping with her. She was twenty when her father died, and since then she had shown a considerable increase in her disability. She had been very attached to her father, and there was probably an unresolved fixation present. Unfortunately she had been granted an invalid pension, and that never was a great aid to the removal of conversion symptoms. She was not a good sleeper, and for a long time had been taking capsules at bed time. She was having a course of carbon dioxide and oxygen anæsthesia therapy, during which short analytic talks were given. The early unfavourable background, the overcare she had had, and the idea that she could not work had all had their effect upon her, and the condition would probably be an obstinate one.

Hysteria with Paraplegia.

The third patient in the group, a single woman, aged twenty-eight years, a clerk, had been admitted to Broughton Hall on October 7, 1949. She was a dissimilar twin; her sister had a different disposition and had been favoured by the mother. The patient followed the lead, and had always done many things to aid her sister. She found herself allowed to do the housework alone. She noticed that boys preferred the sister to her, and, in general, since the death of her father eleven years before, she had been given the task of caring for home and mother without much help. She joined the army to seek relief; but the sister married, and on the patient's discharge from the services the home position had worsened. In the army she had experienced a sore throat, with pain in the neck, and aches had spread all over her body. At the present time she had strange feelings when her chest filled up, her stomach "drew" and she felt as if there was a great void inside her (she had had a similar set of feelings just before her father died), and she walked with difficulty. The history of the present illness would appear to date from that time (eleven years before), and after experiences in the army, she had become worse. She had had a lover formerly, and was engaged to marry, but nothing came of the affair because

he had "dusted lungs" from working in a gold-mine, and he was also completely sexually impotent. There had been another love affair since, but she had permitted only digital stimulation, which she did not like. At the time of the meeting she had an hysterical gait, the right leg being the more affected, and weakness of the right hand with pain when she used it. She lay supine in bed, and made no effort to move about much; but she was mentally alert and pleasant in manner, gave a clear story of her troubles, and did not appear to be unduly troubled by them. She was very incensed, however, at the action of the Repatriation Medical Services in not recognizing her condition as due to war service. Bodily she was healthy enough. The background was not sound, because her father, to whom she was attached, had died suddenly eleven years previously; he collapsed at her brother's twenty-first birthday party and died. He had been an asthmatic and a chronic invalid. The mother was never well, and had made large claims upon the patient's services at home.

The comment was made that the patient was in revolt against the circumstances that had arisen in her home over the years. She was resentful of the freedom of her twin sister, and she had no wish to stay at home and work for the mother and others; yet she was fond of her mother. The conversion symptoms freed her from the immediate execution of those duties, but they had failed to help her army claims, and that fact might stand to her later on when she would have to work for her living. She would have a full course of the carbon dioxide and oxygen therapy, with a series of short psychoanalytical interviews, which would probably give her the social relief sought. The unfortunate love affairs were not in her favour, and there was probably an unresolved father-fixation being experienced. She had formerly used her right hand for improper practices with her impotent lover.

Hysterical Fugue.

The next patient, a married man, aged twenty-eight years, an overseer, had been admitted to the clinic in June, 1949. He had been a very healthy boy with few illnesses. He was of more than average intelligence, and had worked his way to the position of overseer on a country property. He was a bright, talkative person, and his chief failing was that he took too much alcohol. He was married and had a child, and was about to be the father of a second infant. In 1943 he had been in hospital with traumatic neurosis, following a fall from a tram; that condition had lasted for two months. In 1944 he had been in hospital for a month with an anxiety state, having just changed his religion from Baptist to that of his wife—Roman Catholic. He was so disturbed on the day of his wedding at the great prominence of his position as chief performer, after the bride, that he fainted and had to be treated for a month. In 1947 he had entered Broughton Hall for three months treatment for an hysterical fugue state. He had left Quirindi to join his wife in Sydney, but in due course had found that he had gone to Cairns. He had faint recollections of passing through Brisbane to Rockhampton, but was quite unable to recall the business or method of making such a trip. He had been returned to his home by the police, whose aid he enlisted when he found himself in the strange predicament. A little later on he was again on his way to Sydney, but he finally arrived at Perth by aeroplane. He had no recollection of the trip; there was some hazy idea that he had bought the tickets somewhere. He worked in Perth for some days, but was finally put into a mental home and shown at a demonstration as a patient with a fugue state. Finally he was identified and returned to Sydney; until then there was amnesia for the whole event. In 1949 he had made a visit to consult Dr. Lawrance, and when he found that Dr. Lawrance was away, had tried to throw himself over a cliff into the sea, but was restrained and returned to his home. About three weeks prior to his admission to Broughton Hall in June, he had gone to visit a friend who was in the hospital at his home town. The friend died, and the patient had a severe shock. He next found himself wandering about Circular Quay, Sydney, in a dazed condition, having just taken 30 tablets of "Luminal". He had no idea where he was. He was treated for the poisoning at a city hospital, and then was admitted to Broughton Hall. He had been restored to full sanity at the time of the meeting. Dr. Lawrance pointed out that the patient's family background was interesting. His grandfather had been insane; his father had been mentally ill, being both suicidal and homicidal; his brother was an epileptic subject. He did not remember his father, and as a result of being brought up without a male parent, was strongly fixed on his mother. On that account he was more upset than would have been the case otherwise when his mother severely rebuked him for changing his religion. His mother had died recently, and that, too, was a psychological blow to him. He had had a course of electroconvulsive therapy, which helped him, but the improvement did not last; his depression returned, and he was again considered to be a "suicidal risk". He was given a course of carbon dioxide and oxygen narcosis therapy, but he reacted so violently and was so terrified that that had to be discounted. "Sodium Pentothal" intravenous injections were given, and under the influence of these he spoke of love for his mother, of mutual masturbation, and of fellatio taught him by a man in the patient's earlier years. He mentioned that his wife irritated him, and that she did not equal his mother in many respects. He said that there were three great things in his life above all others, namely, his new church, his wife and his doctor. He was given a course of the drug, and short analytical talks as well, after the narcosis induced had passed off. He was better in all ways, he was bright and cheerful, and apparently his mind had been eased of a great tension.

Dr. Lawrance pointed out that Janet claimed that hysteria was due to a malady of synthesis of the personality, with especially a reduction in the field of personal consciousness, dissociation and independent action of the systems of ideas which composed the personality. The deeper the dissociation of consciousness, the more closely did the resultant mental states and their physical expression resemble normal standards. Polyideic somnambulisms were ambulatory automatisms, depending on the dissociation of many more than one system of memories. The ensuing period for which there was amnesis constituted the fugue. Most fugues were based on alcoholism or fear; in the case under discussion the strong repressed material was freed by alcohol, and the patient made definite flights from his fears. The case illustrated the predisposing background and the precipitating factors. The patient's electroencephalogram had some abnormal features not unlike mild epileptic disturbances. Possibly that was the basic weakness; if so he would certainly be facile in his reactions to alcohol, and he did show such effects.

Ataxic Astasia-Abasia.

The last patient of the hysterical group was a married woman, aged forty-two years, who had been admitted to the clinic on June 23, 1949. She had been a healthy person, the mother of four children, her only operation being the removal of hæmorrhoids two years previously. She had myopic vision corrected by glasses. She stated that since the anal operation she had suffered from a pain that passed from that region up into her spine. She said that she could neither sit nor stand because of the pain. She was irritable and had frequent headaches, palpitation of the heart, a pain in the chest and neck, and a dreadful feeling in the head. She had been speaking in a whisper. Her gait was ataxic, but the legs were not weak. There was tremor of the lower limbs, and of the upper to a lesser degree. Investigation revealed a basal metabolic rate of −2%, a normal electrocardiogram, a normal X-ray appearance of the skull and a normal blood count; the diagnosis was made of anxiety hysteria. Her husband was very potent sexually, and she had become frigid owing to her fear of more children, which she did not desire. The unfortunate practice of *coitus interruptus* had been adopted and had been used for years, and the origin of the anxiety was placed there. The family history appeared to be reasonably satisfactory. The patient had been given a course of electroconvulsive therapy with benefit in relation to the anxiety symptoms, and her physical condition had improved considerably. She could sit still on a chair, and she adopted a pose of sitting upright with her knees together and trembling continuously. The gait and the speech had not improved. The patient was to be given a course of narcoanalysis by means of "Pentothal Sodium" given by intravenous injection, when the drug could be purchased again. That therapy would probably resolve her troubles.

Dr. Lawrance remarked that in the case under discussion there was a rift in the marital happiness, the void between the sexual and the frigid. The husband had told him that the patient often scolded him (the husband) for trifles, and that she became extremely unpleasant when he argued with her. The hysterical symptoms had appeared since her hæmorrhoid operation, and there had been some dyspareunia since that time. The symptoms caused her to be sufficiently ill to avoid her fear, namely, another conception, because she had become unable to carry out her part of the programme. She was in hospital; her husband visited her often, and he had become extremely solicitous about her health. Dr. Lawrance quoted the statement of Monrad-Krohn that "in hysteria we find many disturbances of gait, which always show a marked incongruity to the other physical findings, and have a tendency to assume a certain grotesque character". Monrad-Krohn mentioned paralytic

astasia-abasia, in which the patient fell limply down on standing, and ataxic astasia-abasia, in which the patient carried out all sorts of jerky involuntary movements, being on the point of falling, and on the whole walking on the floor as if he was balancing on a tight-rope. The patient had conformed to that type on arrival at the clinic, but there had been some improvement since then. The chief trouble was that when she went home the same set of provocative life-situations would be before her. The husband was not sympathetic to any explanations of her illness, and claimed that she was just a contrary woman. The patient was having a course of carbon dioxide and oxygen inhalation therapy, and improvement was looked for soon.

(To be continued.)

Medical Practice.

POLIOMYELITIS.

Movement of Patients in the Acute Stage.

THE Victorian Consultative Council on Poliomyelitis desires to remind practitioners, particularly in the country, of the danger in transporting poliomyelitis patients for long distances while in the acute stage of the disease. It has been demonstrated that muscle fatigue in the acute stage is a potent cause of extension of paralysis. Several recent examples have shown that fatigue associated with a long journey has similar bad effects.

The Council therefore advises that patients in the early stage of poliomyelitis should be moved no further than to the nearest hospital at which facilities are available. If a long journey to hospital is unavoidable, the patient should be transported in a comfortable ambulance, bad roads should be avoided, and unless there are signs of paralyses dangerous to life, there should be no necessity for speed, and frequent rests should be taken.

The following signs indicate development of dangerous paralyses: (i) nasal tone to the voice, (ii) difficulty in swallowing, (iii) bubbling mucus in throat and lungs, (iv) a weak cough, (v) inability to expand the chest, (vi) rapid onset of paralysis of arms (often indicating a rapid extension to the respiratory muscles particularly in adults).

POLIOMYELITIS AND ROUTINE TONSIL AND ADENOID OPERATIONS.

THE following statement is published at the request of the Consultative Council for the Physically Handicapped:

In view of the recent increase of cases of poliomyelitis within the last few days, it is the opinion of this Council that the danger of contracting a bulbar form of poliomyelitis is definitely greater in persons who have recently undergone removal of adenoids and tonsils than in the community in general, and this Council advises that during the currency of the present poliomyelitis epidemic, such operations should be performed only in cases where postponement carries a considerable risk to the person's health.

Special Correspondence.

NEW ZEALAND LETTER.

FROM OUR SPECIAL CORRESPONDENT.

THE National Party was returned with the substantial majority of 46 seats to Labour's 34, the latter figure including all the four Maori seats. The Labour Government's fourteen years of office thus came to an end and Mr. S. G. Holland assumes the task of Prime Minister. The new Minister of Social Security and Health is Mr. J. T. Watts, of Christchurch, a barrister and solicitor of about forty years of age, with a distinguished academic record, who entered Parliament first six years ago. Mrs. Hilda Ross, of Hamilton, is Minister without Portfolio and Minister for the Welfare of Women and Children. Mr. R. M. Algie, a former Professor of Law at Auckland University College, is Minister of Education.

The National Party's election policy emphasized prevention and research, and promised a complete reorganization of the hospital system on a basis of regional control and decentralization. It supported recent Acts for the more economical management of medical and pharmaceutical benefits, and promised help for the elderly, for the Post-Graduate Women's Teaching Hospital in Auckland, and a number of other projects.

With recent and forthcoming appointments inside the Health Department, notably that of the new Director-General, Dr. J. Cairney, the field is open for much needed progressive development.

The Labour Party's fourteen years saw the introduction, in spite of war-time difficulties, of an almost complete series of medical and allied benefits under Social Security, specialist services being the only major gap. The fee-for-service principle in maternity and medical benefits was dominant. Little change in hospital organization and planning was undertaken, though the Government came to be much more responsible for finance than formerly, during this era.

Obituary.

James Fitzsimons, M.B. (N.Z.), F.R.C.S. (England), F.R.A.C.S., died suddenly in Auckland on December 10, 1949, at the age of fifty-two. He had had a heart attack last August and had seemingly recovered well, though he had not resumed practice.

Educated at Waitaki Boys' High School and Otago University, where his course was distinguished, culminating in winning the travelling scholarship for his year, he pursued post-graduate studies in England, taking his F.R.C.S. in 1927. He returned to New Zealand as resident surgical officer to Dunedin Hospital, and commenced practice in Auckland in 1929. Appointments as assistant and later full visiting surgeon to Auckland Hospital were held in conjunction with a busy surgical practice. His chief interest was in gastro-enterology. He visited the United States of America in 1939. He was a member of the Branch Medical Faculty in Auckland and of the Post-Graduate Committee, and was greatly interested in the final year medical students. Mr. Fitzsimons is survived by his wife, two daughters and a son.

Correspondence.

JOHN IRVINE HUNTER MEMORIAL LECTURE.

SIR: The committee of the John Irvine Hunter Memorial Lecture have been fortunate in securing Professor Raymond Dart, of Johannesburg, to deliver the inaugural oration on January 31 in the Wallace Theatre of the University of Sydney at 8 p.m. The Chancellor will preside.

Professor R. Dart is a distinguished graduate of Queensland (M.Sc.) and Sydney (M.D., Ch.M.) Universities. He served in the first World War after doing research work in Sydney under the late Professor J. T. Wilson and early in 1920 worked under Professor Sir Grafton Elliot-Smith at University College. While here Dart and Hunter were fellow students under Elliot-Smith. Later, he went to the University of the Witwatersrand, and while acting as Dean of the Faculty of Medicine there, he built up an international reputation for his discoveries of the "Fossil Ape Men" of South Africa, including the Taungs skull *et cetera*, and invented a new word, the "Australopithecinæ", for this family of man apes.

The steadily accumulating evidence, at first looked upon somewhat askance by some scientists, shows that they walked upright like man, having a human femur and hip bone, and were about four feet in height; they also had a smallish brain but human teeth, a human thumb, and, finally, they hunted and killed baboons and used fire. Thus, a most remarkable picture has been built up by the painstaking researches of Dart, Broom and their colleagues.

Members of the medical profession and, particularly, colleagues of the late Professor Hunter or of Professor Dart himself, are cordially invited to the lecture and are asked to apply for tickets to the Sydney University Extension Board or the Department of Anatomy, University of Sydney.

Yours, etc.,

A. L. BURKITT,
Professor of Anatomy.

The University of Sydney,
Sydney,
January 18, 1950.

THE PAINFUL STIFF SHOULDER.

SIR: I was very interested to see Dr. A. T. Pearson's letter in THE MEDICAL JOURNAL OF AUSTRALIA, December 24, 1949, concerning the pathogenesis of the common variety of painful stiff shoulder. In my address, owing to limitation of time, I did not probe at any length into this interesting problem, about which there is much discussion.

There is, however, one misconception which I feel should be corrected. The term "adhesions", perhaps rather loosely applied in this case, refers to a purely periarticular condition in which changes occur in the capsule and adjacent soft tissues and not within the joint itself. Most will agree that the condition is peri- and not intra-articular, and although there may be some differences between Dr. Pearson and myself regarding terminology, there is none so far as the actual findings are concerned. I am in full agreement with him on this point. His theory of pathogenesis is a logical one with which many would agree, and I am indebted to him for bringing out a more detailed discussion on this aspect.

However much discussion there may be regarding the primary lesion, whether it be "bursitis", "tendonitis" or "fibrositis" *et cetera*, it is probable that any painful condition in the region of the shoulder joint results in the joint being kept at rest, which is so easily done by holding the arm to the side. It is probable, therefore, that a variety of primary conditions result in the arm being kept dependent, with the resultant sequelæ that Dr. Pearson has described.

His suggestion of altering the aphorism, "a movement a day keeps the adhesions away", to "a movement a day keeps the spasms and shortening away", is of interest in so far as it directs attention to the protective shortening and spasm which precedes later organic changes.

Yours, etc.,
L. T. WEDLICK.

41 Spring Street,
Melbourne, C.1,
December 29, 1949.

Obituary.

THE J. W. GRIEVE MEMORIAL LIBRARY.

IN the board room at the Children's Hospital, Melbourne, on Thursday, December 15, 1949, a solemn ceremony took place to dedicate the medical library as a memorial to the late Dr. John Whyte Grieve. Mrs. Grieve and her three daughters and also Mr. Bob Grieve, V.C., brother of the late John Whyte Grieve, were present, together with a large gathering representative of the committee of management and past and present colleagues on the staff of the hospital and a group of other people who wished to share in the ceremony.

Lady Latham, President of the hospital, said that they were met together to honour the memory of Dr. John Whyte Grieve, and to name the medical library of the Children's Hospital, wherever the hospital might be situated, the J. W. Grieve Memorial Library. The occasion was a moving one, for it seemed only yesterday that they had all been working with Dr. Grieve and were abundantly strengthened by his judgement, his high ideals and his devotion to their common cause of making sick children well.

Dr. Grieve had given the hospital twenty-nine years of oustanding service—at first in junior positions, then as honorary physician attending in-patients, a position which he held for twenty-three years. In 1944 he was elected to the committee of management and had remained a member of that body until his death.

An extract from the minutes read as follows:

> The committee of management of the Children's Hospital records with deep regret and profound sorrow the death of Dr. J. W. Grieve. Dr. Grieve gave this hospital twenty-nine years of outstanding service, at first in junior positions and then as honorary attending physician to in-patients, a position which he held for twenty-three years until his retirement in March of this year.
>
> At the time of his death he was still a member of the committee of management.
>
> His work in the hospital will long be remembered by all who worked with him and by those for whom he worked, by committee members, members of the honorary medical staff, the administrative and nursing sides of the hospital as well as by the patients and their parents, and by the medical students to whom he gave not only valuable clinical instruction but also the inspiration of his wise and unselfish personality.
>
> As a member of the committee of management Dr. Grieve proved himself a most valuable colleague, and during his all-too-short period of service his great knowledge and experience of the intricate problems of hospital management were of inestimable value.

Dr. Boyd Graham, formerly chairman of the medical staff, and Dr. Reginald Webster, Mary and Evelyn Burton Research Fellow, both of them life-long friends and fellow workers with Dr. Grieve, would add their tributes to his memory.

Dr. H. Boyd Graham said that it was his very great privilege to represent the medical staff of the Children's Hospital at the dedication ceremony when they were making an imperishable memorial to the well-loved comrade, the late Dr. John Whyte Grieve.

Jock and he had been close friends and had served alongside each other at the hospital from January 4, 1920, till his death in the previous year. Grieve had been their leader all through those years. At a relatively early age he became a physician to in-patients and for several years had been the senior physician. He possessed the qualities of leadership. He was high-principled and courageous, steadfast, dependable, genial but unostentatious, well informed and very wise. He displayed those qualities early and his character, judgement and influence developed as an avalanche grew.

He had entered the Preparatory School at Wesley College in 1904 and in the following year he was captain of cricket, captain of football and *dux* of the school. In the senior school he was a form captain and later a prefect and a member of the cricket team. In 1916 he topped off his medical course at the University of Melbourne by gaining second-class honours in all subjects and sharing the Beaney Scholarship in Surgery.

Grieve served with the Ninth Battalion of the Australian Imperial Force in the 1914-1918 war as a captain in the Australian Army Medical Corps and was mentioned in dispatches.

In 1919 he commenced his memorable career at the Children's Hospital as a resident medical officer together with some wartime comrades, including Fred Le Messurier, Ralph Crisp, Vernon Brown and Elliot True, and when

Le Messurier left in 1920 Jock became the senior resident. Early in 1922 he left the resident medical staff and rapidly obtained out-patient appointments at the Children's Hospital and Saint Vincent's Hospital and started in private practice in Collins Street. He was soon inundated with work, but undertook additional honorary service for many years for Saint Gabriel's Babies' Home, the After-Care Hospital and the District Nursing Society.

He married and became the model husband and devoted father of a charming family and he revelled in the joys of the home. He had the happy temperament that rushed to meet the confiding moods of little children and the wonderful patience that overcame all aggression and distrust. For many years his rugged, solid physique had taken the enormous strain without flinching, but ultimately his health became the subject of some anxiety for his friends and relations. Throughout the recent war he had been a constant visiting consultant at the Heidelberg Military Hospital and served on innumerable medical boards.

He had been sensible enough to take holiday breaks with his growing children, but at the last he had gone so suddenly that all were stunned and shocked—the medical staff lost its mainstay; the Melbourne Pædiatric Society lost its general factotum; the committee of management lost its active medical member and trusted technical adviser; the Faculty of Medicine lost one of its chief examiners in general medicine and in pædiatric medicine.

It had taken them over a year to realize that he had gone, but his influence remained and would be perpetuated through the library which was his dream. He was very studious and shamed them all by the way in which he managed to keep up with the essential medical literature. Of course, he was a Foundation Fellow of the Royal Australasian College of Physicians and naturally he was a great teacher of medical students and nurses. The Children's Hospital was justly proud of its great physicians. From Snowball through Stawell, Hobill Cole, Jeffreys Wood and Stewart Ferguson they came to Jock Grieve. What a glorious heritage they had handed on! Let those who followed prove worthy of them!

Dr. Reginald Webster said that he counted it a high privilege to speak in appreciation of a friend and colleague of many years, the number of which might be calculated from the fact that the late Dr. Grieve, Mr. Robert Grieve and he (Dr. Webster) were contemporaries at Wesley College. On many occasions during the period of his association with the hospital had "Jock" Grieve and he jointly defended the old school in the good-natured raillery which seemed to be generated by a process of spontaneous combustion whenever the members of a group became school conscious.

Dr. Webster said that he had therefore been well situated to observe the successive stages by which, as his innate sterling qualities developed and matured, he whom they were assembled together to honour evolved from a junior school boy into a consulting physician of high repute, and a wise and stable counsellor in the complex problems of hospital management.

Dr. Webster had always regarded Dr. Grieve as an exponent of the scientific method in medical practice. There was a widespread impression in the public mind, and one of which Dr. Webster was afraid many members of the medical profession had not divested themselves, that scientific medicine was inseparable from the laboratory. This, he would submit, was a fallacy. Science in medicine was an intellectual method and did not reside in an impressive array of laboratory equipment or in facility in surmounting the difficulties of an intricate technique.

In that he invariably approached a clinical problem by the meticulously careful assembly of all the ascertainable facts, subjected such data to critical analysis, and brought to bear a penetrating insight which enabled him to sift the wheat from the chaff in an involved clinical story, Dr. Grieve had expounded the scientific method in no less degree than the laboratory worker who studied the behaviour of the cells of human tissues in artificial culture, or was led by the occurrence of anomalous reactions in a random and fortuitous sample of blood into a long and patient investigation which culminated in the discovery of a new blood group.

At meetings of the Melbourne Pædiatric Society, of which body he was for many years the indefatigable honorary secretary, Dr. Grieve's presentations of diagnostic problems were made consistently in the manner of one who placed first things first and realized the fundamental importance of a full and accurate clinical history, without which indeed the structure of diagnosis was likely to be as the house built upon the sand in the New Testament parable, prone to totter and collapse.

The present library was but the nucleus of that envisaged for the new hospital, the guiding principle in the planning of which would be to ensure that it was designed on adequate lines, that it might grow in future usefulness and dignity, and in its growth sustain the lustre of the name with which those present endowed it in the early stage of its development.

How appropriate to the character of the man to whom they dedicated it that day was the library! Of the essence of a library was an atmosphere of calm and serenity, in which knowledge might be sought for its own sake, ideas might be weighed in the balance of contemporary opinion, and assistance obtained in the solution of difficult and perhaps pressing problems. Dr. Webster had no doubt that all his colleagues of a period irrevocably closed would agree that the qualities suggested by a library were all to be found in the personality of J. W. Grieve, as witnessed his even temperament, his reflective disposition, imperturbability under stress—he was blessed with the *"Æquanimitas"* of Osler in high degree—and his store of knowledge and wisdom, freely drawn upon by both senior and junior colleagues.

A cherished objective of all concerned in moulding the character of the hospital, shared equally by the committee of management and the honorary medical staff, was that it should establish itself as an educational centre of note, and attain renown in all matters relating to child health. To this ideal Dr. Grieve had been devoted, and in his capacities of representative of the Children's Hospital on the Faculty of Medicine in the University of Melbourne, and on the Melbourne Permanent Post-Graduate Committee, he had worked with singleness of purpose to promote it. Those present should entertain no doubt that in the fullness of time the hospital would be acclaimed as the Mecca of all in the Southern Hemisphere who would seek first a knowledge of children, and the illnesses of body and mind which might overtake them. But even though the hospital became a great post-graduate centre, and attained preeminence as a clinical school, the index of its greatness would be found, not in its imposing buildings, not in the munificence of its endowments, not in the profusion of its equipment in special departments such as those of pathology and radiology, but in the names of the men and women who laboured with unremitting devotion to advance the status of the institution to which they were so deeply attached. Just as no amount of gilt edging could determine the quality of the books in the Memorial Library, no splendour of exterior, nor any measure of "pride, pomp, and circumstance" could ensure greatness to a hospital which lacked men and women of ability, vision, and self-sacrificing enthusiasm. The pride of a clinical school, as Sir William Osler had said of a university, was centred in the names of its great men, and without doubt, in the traditions of the Children's Hospital, the name of John Whyte Grieve would be one of those that would be accounted great.

Lady Latham said that it was her duty and privilege to name the medical library of the Children's Hospital "The J. W. Grieve Memorial Library" and to direct that the tablet which was on view should be suitably placed at the entrance or within the present library and later be moved with the library itself to its permanent home in the new hospital.

In the name of them all, she dedicated the library to the memory of Dr. J. W. Grieve.

JOSEPH FOREMAN.

WE regret to announce the death of Dr. Joseph Foreman, which occurred on January 15, 1950, at Sydney.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

McRae, Margaret Ruth, provisional registration, 1949 (Univ. Sydney), 31 Vaucluse Road, Vaucluse.

Lance, James Waldo, provisional registration, 1949 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

Ross, Judith May, provisional registration, 1949 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Brierley, June Cooper, provisional registration, 1949 (Univ. Sydney), Balmain District Hospital, Balmain.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 31, 1949[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	•	4(4)	..	..	..	..	..	..	4
Anthrax	•	..	..	..	..	..	..	..	..
Beriberi	•	•	•	•	•	•	..	•	..
Bilharziasis	•	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	4(3)	2(2)	1(1)	..	..	..	..	..	7
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	•	•	..	•	•	•	•	•	..
Dengue	•	•	•	•	•	•	..	•	..
Diarrhœa (Infantile)	..	..	1(1)	..	1	..	..	..	2
Diphtheria	7(7)	2(1)	3(2)	..	1(1)	..	..	..	13
Dysentery (Amœbic)	•	1(1)	..	..	..	..	..	..	1
Dysentery (Bacillary)	•	..	3(2)	..	..	..	..	..	3
Encephalitis Lethargica	..	..	..	..	•	..	..	..	..
Erysipelas	•	•	•	..	..	..	..	..	..
Filariasis	•	..	•	•	•	•	•	•	..
Helminthiasis	•	..	..	•	..	•	•	..	..
Hydatid	•	..	•	..	•	•	..	•	..
Influenza	•	•	..	•	•	•	•	•	..
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	•	..	..	1	1	..	..	..	1
Measles	•	•	•	17	•	•	..	..	17
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	14(3)	13(5)	..	30	..	..	..	..	57
Psittacosis	•	..	..	..	..	..	..	..	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella(*c*)	•	•	4(2)	•	..	•	..	..	4
Scarlet Fever	12(8)	13(8)	8(7)	5	2(1)	..	..	..	40
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	•	..	..	•	•	•	•	•	..
Trachoma	•	..	..	•	..	•	•	•	..
Tuberculosis(*d*)	4(2)	10(6)	6(6)	4	15(13)	..	..	..	39
Typhoid Fever(*e*)	..	..	..	..	1(1)	..	..	..	1
Typhus (Endemic)(*f*)	..	..	1	..	1(1)	..	..	..	2
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	•	•	..	•	•	•	•	•	..
Whooping Cough	•	•	•	11	•	•	..	..	11
Yellow Fever	..	..	..	..	..	..	..	..	..

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JANUARY 7, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.[2]	Australian Capital Territory.	Australia.[3]
Ankylostomiasis	•	1(1)	..	..	..	..	..	..	1
Anthrax	•	..	..	..	..	..	..	..	..
Beriberi	•	•	•	•	•	•	..	•	..
Bilharziasis	•	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	1(1)	1(1)	..	..	2(1)	..	..	..	4
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	•	•	..	•	•	•	•	•	..
Dengue	•	•	•	•	•	•	..	•	..
Diarrhœa (Infantile)	..	..	21(17)	..	..	..	..	..	21
Diphtheria	7(2)	2(2)	9(6)	..	3(2)	..	..	..	21
Dysentery (Amœbic)	•	1	..	..	..	..	..	..	1
Dysentery (Bacillary)	•	..	7(7)	..	..	..	..	..	7
Encephalitis Lethargica	1(1)	..	..	..	..	..	..	..	1
Erysipelas	•	•	•	..	•	•	..	..	..
Filariasis	•	..	..	..	..	..	..	..	..
Helminthiasis	•	..	•	•	•	•	•	•	..
Hydatid	•	..	•	•	..	•	•	..	..
Influenza	•	•	..	..	•	•	•	•	..
Lead Poisoning	•	•	•	..	•	•	..	•	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	•	..	..	..	..	..	..	..	..
Measles	•	•	•	15(13)	•	•	..	..	15
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	11(7)	15(7)	..	35(26)	..	3	..	..	64
Psittacosis	•	..	•	..	..	•	•	•	..
Puerperal Fever	..	..	..	1(1)	..	..	..	..	1
Rubella(*c*)	..	..	1(1)	•	..	2	..	..	3
Scarlet Fever	21(10)	31(12)	6(4)	10(2)	..	3(1)	..	..	71
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	•	..	2(1)	•	•	•	•	•	2
Trachoma	•	..	•	..	..	..	..	..	..
Tuberculosis(*d*)	15(11)	8(7)	9(5)	6(4)	8(4)	5(3)	..	..	51
Typhoid Fever(*e*)	1	2	..	..	..	..	..	..	3
Typhus (Endemic)(*f*)	..	..	..	..	..	..	..	..	..
Undulant Fever	..	1	..	..	..	..	..	..	1
Weil's Disease(*g*)	•	•	•	•	•	•	•	•	..
Whooping Cough	•	•	•	24(7)	•	•	..	..	24
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from the Northern Territory.

• Not notifiable.

(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Woods, William Cleaver, provisional registration, 1949 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
Wilson, Jean Margaret, M.B., B.S., 1947 (Univ. Sydney), 132 Glebe Road, Glebe.
Cohen, Stanley Victor, M.B., B.S., 1948 (Univ. Sydney), 25 O'Brien Street, Bondi.
Hann, Lionel Frederick, provisional registration, 1949 (Univ. Sydney), St. George Hospital, Kogarah.

The undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

McRobert, Helen Angus, M.B., B.S., 1949 (Univ. Adelaide), 225 Portrush Road, Glenunga.
Seith, Wolfram Immanuel, M.B., B.S., 1949 (Univ. Adelaide), 41 Lambert Road, Joslin.
Plueckhahn, Vernon Douglas, M.B., B.S., 1949 (Univ. Adelaide), 73 Mills Street, Clarence Park.
Last, John Murray, M.B., B.S., 1949 (Univ. Adelaide), 7 Olive Street, Glenelg.
Ducray, Suzette Eleanor, M.B., B.S., 1949 (Univ. Adelaide), Royal Adelaide Hospital, Adelaide.
Simpson, Donald Allen, M.B., B.S., 1949 (Univ. Adelaide), 42 Lockwood Road, Burnside.
Nicholls, Edward Maxwell, M.B., B.S., 1949 (Univ. Adelaide), Darwin Hospital, Darwin.
Souter, Douglas Tod, M.B., B.S., 1949 (Univ. Adelaide), 258 Glen Osmond Road, Fullarton.
Kerr, Grant Allen, M.B., B.S., 1947 (Univ. Adelaide), 87 Park Terrace, North Unley.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association:

Lappin, Frank, provisional registration, 1949 (Univ. Sydney), Parramatta District Hospital, Parramatta.
McDonald, George Roy William, provisional registration, 1949 (Univ. Sydney), 93 Victoria Road, Bellevue Hill.
Rosengarten, Lionel, provisional registration, 1949 (Univ. Sydney), Flat 10, 69 Birriga Road, Bellevue Hill.
Schiller, Eric, M.B., B.S., 1948 (Univ. Sydney), 9 Killarney Street, Mosman.
Watson, Keith Gordon, M.B., B.S., 1948 (Univ. Sydney), 21 Parriwi Road, Mosman.
Winkworth, Alan Charles Stepney, M.B., B.S., 1948 (Univ. Sydney), 19 Kylie Avenue Killara.
Perkins, Ronald George, M.B., B.S., 1947 (Univ. Sydney), 7 Ayr Street, Ashbury.
Hewer, George Frederick, M.B., Ch.M., 1919 (Univ. Sydney), Narromine, New South Wales.

University Intelligence.

THE UNIVERSITY OF SYDNEY.

John Irvine Hunter Memorial Lecture.

THE inaugural John Irvine Hunter Memorial Lecture will be given by Professor Raymond Dart, M.Sc., M.D., Ch.M., on "Fossil Man Apes of South Africa and Their Bearing on Human Evolution" on Tuesday, January 31, 1950, at 8 p.m. in the Wallace Theatre, at the University of Sydney. Admission will be by ticket obtainable on application to the Sydney University Extension Board or the Department of Anatomy. Former colleagues of Professor Hunter and Professor Dart will be particularly welcome.

Notice.

DEMONSTRATION OF TELEVISION.

FROM Tuesday, February 7, to Friday, February 10, 1950, inclusive, by courtesy of Amalgamated Wireless (Australasia), Limited, demonstrations of television at Sydney Hospital have been arranged. These demonstrations, lasting sixty to seventy-five minutes each day, will include a varied selection of medical and surgical subjects. All medical practitioners are invited to attend; full details of times, subjects *et cetera* may be obtained by telephoning the medical superintendent's office at Sydney Hospital.

Medical Appointments.

Dr. G. R. West has been appointed honorary consulting medical officer, Northfield Wards, at the Royal Adelaide Hospital, Adelaide.

Dr. J. A. Bonnin has been appointed clinical pathologist at the Institute of Medical and Veterinary Science, Adelaide.

Diary for the Month.

JAN. 28.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 1.—Western Australian Branch, B.M.A.: Council Meeting.
FEB. 1.—Victorian Branch, B.M.A.: Branch Meeting.
FEB. 2.—South Australian Branch, B.M.A.: Council Meeting.
FEB. 3.—Queensland Branch, B.M.A.: Branch Meeting.
FEB. 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.
FEB. 10.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135 Macquarie Street, Sydney): Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester United Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £3 *per annum* within Australia and the British Commonwealth of Nations, and £4 10s. *per annum* within America and foreign countries, payable in advance.